

WEST Search History

10/018704

DATE: Thursday, August 14, 2003

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DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ

L12	L11 and (malaria or plasmodium or parasit\$ or rts or trap)	8	L12
L11	L10 and cpg	11	L11
L10	immunomodulatory oligonucleotide	20	L10
L9	l4 and immunomodulatory oligonucleotide	0	L9
L8	l4 and immunomodulatory adj4 oligonucleotid\$	0	L8
L7	l4L6	9	L7
L6	l4 and (malaria or plasmodium or parasit\$)	13	L6
L5	L4 and cpg	1	L5
L4	l1 or l2 or L3	51	L4
L3	voss-gerald.in.	3	L3
L2	garcon-nathalie.in.	19	L2
L1	cohen-joseph.in.	29	L1

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NEWS 19 May 19 Simultaneous left and right truncation added to WSCA
NEWS 20 May 19 RAPRA enhanced with new search field, simultaneous left and
right truncation
NEWS 21 Jun 06 Simultaneous left and right truncation added to CBNB
NEWS 22 Jun 06 PASCAL enhanced with additional data
NEWS 23 Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS 24 Jun 25 HSDB has been reloaded
NEWS 25 Jul 16 Data from 1960-1976 added to RDISCLOSURE
NEWS 26 Jul 21 Identification of STN records implemented
NEWS 27 Jul 21 Polymer class term count added to REGISTRY
NEWS 28 Jul 22 INPADOC: Basic index (/BI) enhanced; Simultaneous Left and
Right Truncation available
NEWS 29 AUG 05 New pricing for EUROPATFULL and PCTFULL effective
August 1, 2003
NEWS 30 AUG 13 Field Availability (/FA) field enhanced in BEILSTEIN

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=> e garcon nathalie/au

E1	3	GARCON N M J/AU
E2	3	GARCON N M J C/AU
E3	38 -->	GARCON NATHALIE/AU
E4	3	GARCON NATHALIE M/AU
E5	1	GARCON NATHALIE M J/AU
E6	5	GARCON NATHALIE MARIE JOSEPHE/AU
E7	4	GARCON NATHALIE MARIE JOSEPHE CLAUDE/AU
E8	1	GARCON O/AU
E9	12	GARCON P/AU
E10	3	GARCON PH/AU
E11	4	GARCON R/AU
E12	8	GARCON S/AU

=> s e1-e7

L1 57 ("GARCON N M J"/AU OR "GARCON N M J C"/AU OR "GARCON NATHALIE"/A
U OR "GARCON NATHALIE M"/AU OR "GARCON NATHALIE M J"/AU OR "GARC
ON NATHALIE MARIE JOSEPHE"/AU OR "GARCON NATHALIE MARIE JOSEPHE

CLAUDE"/AU)

=>

=> e cohen joseph/au

E1	36	COHEN JOSE L/AU
E2	2	COHEN JOSEF/AU
E3	119 -->	COHEN JOSEPH/AU
E4	1	COHEN JOSEPH D/AU
E5	1	COHEN JOSEPH DAVID/AU
E6	7	COHEN JOSEPH H/AU
E7	6	COHEN JOSEPH H III/AU
E8	1	COHEN JOSEPH JACOB 1878 1953/AU
E9	9	COHEN JOSEPH L/AU
E10	1	COHEN JOSEPH M/AU
E11	1	COHEN JOSEPH PERRY/AU
E12	6	COHEN JOSEPH S/AU

=> s e3

L2 119 "COHEN JOSEPH"/AU

=> e voss gerald/au

E1	1	VOSS GEORGE F/AU
E2	2	VOSS GEORGE W/AU
E3	73 -->	VOSS GERALD/AU
E4	4	VOSS GERD/AU
E5	13	VOSS GERHARD/AU
E6	2	VOSS GERHARD R/AU
E7	1	VOSS GERHARD REINER/AU
E8	1	VOSS GERLING WILHELM/AU
E9	5	VOSS GERRIT/AU
E10	2	VOSS GESCHE M/AU
E11	4	VOSS GILBERT L/AU
E12	1	VOSS GLENN/AU

=> s e3

L3 73 "VOSS GERALD"/AU

=> s l1-l3

L4 246 (L1 OR L2 OR L3)

=> s l4 and cpg

L5 8 L4 AND CPG

=> dup rem l5

PROCESSING COMPLETED FOR L5

L6 8 DUP REM L5 (0 DUPLICATES REMOVED)

=> d bib ab 1-8

L6 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:282425 CAPLUS

DN 138:302637

TI Intradermal vaccine compositions comprising saponin, sterol, and LPS derivative or **CpG** oligonucleotide as adjuvant

IN **Garcon, Nathalie**

PA Glaxosmithkline Biologicals S.A., Belg.

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.

KIND DATE

APPLICATION NO. DATE

PI WO 2003028760 A2 20030410 WO 2002-EP10931 20020930
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-23580 A 20011001

AB The present invention provides novel intradermal vaccines and novel uses for adjuvants in the prepn. of intradermal vaccines, and also novel methods of treatment comprising them. The intradermal adjuvants, and methods, of the present invention comprise a saponin and a sterol, wherein the saponin and sterol are formulated in a liposome. The intradermal vaccine further comprises a LPS deriv. or an immunostimulatory **CpG** oligonucleotide. The intradermal adjuvants are used in the manuf. of intradermal vaccines for humans, and in the intradermal treatment of humans.

L6 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:117661 CAPLUS

DN 138:168809

TI Vaccine comprising gp120 and Nef and/or Tat for the immunization against HIV

IN Ertl, Peter Franz; Tite, John Philip; Van Wely, Catherine Ann; **Voss, Gerald**

PA Glaxosmithkline Biologicals S.A., Belg.; Glaxo Group Limited

SO PCT Int. Appl., 108 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2003011334 A1 20030213 WO 2002-EP8343 20020726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2001-18367 A 20010727

AB The invention concerns use of (a) an HIV Tat protein or polynucleotide; or (b) an HIV Nef protein or polynucleotide; or (c) an HIV Tat protein or polynucleotide linked to an HIV Nef protein or polynucleotide; and an HIV gp 120 protein or polynucleotide in the manuf. of a vaccine suitable for a prime-boost delivery for the prophylactic or therapeutic immunization of humans against HIV, wherein the protein or polynucleotide is delivered via a bombardment approach. The vaccines were shown to induce antibody and cytotoxic T-cell responses.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2003:276663 CAPLUS
 DN 138:302632
 TI Adjuvant compns. and uses thereof in vaccines
 IN Friede, Martin; **Garcon, Nathalie**; Gerard, Catherine Marie
 Ghislaine; Hermand, Philippe
 PA Smithkline Beecham Biologicals S.A., Belg.
 SO U.S., 29 pp., Cont.-in-part of Appl. No. PCT/EP00/02920.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6544518	B1	20030408	US 2000-690921	20001018
	US 6558670	B1	20030506	US 1999-301829	19990429
	WO 2000062800	A2	20001026	WO 2000-EP2920	20000404
	WO 2000062800	A3	20010111		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	WO 2002032450	A2	20020425	WO 2001-EP11984	20011016
	WO 2002032450	A3	20021010		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
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	AU 2002044337	A5	20020429	AU 2002-44337	20011016
	EP 1326638	A2	20030716	EP 2001-987671	20011016
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	GB 1999-8885	A	19990419		
	US 1999-301829	A2	19990429		
	WO 2000-EP2920	A2	20000404		
	GB 2000-25573	A	20001018		
	GB 2000-25574	A	20001018		
	US 2000-690921	A	20001018		
	WO 2001-EP11984	W	20011016		

AB The present invention relates to adjuvant compns. which are suitable to be used in vaccines. In particular, the adjuvant compn. of the invention comprises a saponin and an immunostimulatory oligonucleotide, optionally with a carrier. Also provided by the disclosed invention are vaccines comprising the adjuvants of the present invention and an antigen. Further provided are methods of manuf. of the adjuvants and vaccines of the present invention and their use as medicaments. Methods of treating an individual susceptible to or suffering from a disease by the administration of the vaccines of the present invention are also provided.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2002:849463 CAPLUS

DN 137:336724
 TI Vaccine comprising human immunodeficiency virus antigens and human papillomavirus and/or herpes simplex virus antigens
 IN Debrus, Serge; Mathy, Nathalie Louise; **Voss, Gerald**
 PA Glaxosmithkline Biologicals S.A., Belg.
 SO PCT Int. Appl., 34 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002087614	A2	20021107	WO 2002-EP4966	20020425
	WO 2002087614	A3	20030424		
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	RW:				
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PRAI GB 2001-10431 A 20010427

AB The present invention relates to a vaccine compn. comprising at least one human immunodeficiency virus (HIV) antigen and either one or both of: (i) at least one herpes simplex virus (HSV) antigen and (ii) at least one human papillomavirus (HPV) antigen. The HIV antigen can be selected from the group consisting of gpl60, gpl20, nef, tat, a nef-tat fusion protein, gag, or pol. The HSV antigen can be gD glycoprotein, and the HPV antigen can be L1, L2, E6 and/or E7 proteins. The vaccine further comprises a Th1-inducing adjuvant such as 3D-MPL, QS-21, cholesterol, and/or Cpg oligodeoxynucleotides.

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:314785 CAPLUS

DN 136:339479

TI Vaccines comprise cancer antigen and saponin and immunostimulatory oligonucleotide

IN **Garcon, Nathalie**; Gerard, Catherine Marie Ghislaine; Stephenne, Jean

PA Smithkline Beecham Biologicals SA, Belg.

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032450	A2	20020425	WO 2001-EP11984	20011016
	WO 2002032450	A3	20021010		
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	RW:				
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	US 6544518	B1	20030408	US 2000-690921	20001018
	AU 2002044337	A5	20020429	AU 2002-44337	20011016

EP 1326638 A2 20030716 EP 2001-987671 20011016
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI GB 2000-25573 A 20001018
 GB 2000-25574 A 20001018
 US 2000-690921 A 20001018
 GB 1999-8885 A 19990419
 US 1999-301829 A2 19990429
 WO 2000-EP2920 A2 20000404
 WO 2001-EP11984 W 20011016

AB The present invention provides novel adjuvant formulations for use with cancer antigens. The cancer antigen is MAGE, P5015, Cripto, Her 2 neu, prostase or derivs, or their fusion protein. The adjuvant comprises a saponin (e.g. QS21, or ISCOMs) and an immunostimulatory **CpG** -contg. oligonucleotide. The adjuvant may further comprise a lipopolysaccharide such as monophosphoryl lipid A, 3-O-deacylated monophosphoryl lipid A, or disphosphoryl lipid A.

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2001:12292 CAPLUS

DN 134:85122

TI Vaccine

IN **Garcon, Nathalie; Voss, Gerald**

PA Smithkline Beecham Biologicals S.A., Belg.

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000232	A2	20010104	WO 2000-EP5998	20000628
	WO 2001000232	A3	20010525		
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EP 1198249	A2	20020424	EP 2000-943919	20000628	
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WO 2001054719	A2	20010802	WO 2001-EP944	20010129	
WO 2001054719	A3	20011220			
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BR 2001007972	A	20021105	BR 2001-7972	20010129	
NO 2002003616	A	20020917	NO 2002-3616	20020730	
PRAI GB 1999-15205	A	19990629			
GB 2000-2200	A	20000131			

GB 2000-9336 A 20000414
GB 2000-13806 A 20000606
WO 2000-EP5998 W 20000628
WO 2001-EP944 W 20010129

AB A vaccine formulation for the prevention or amelioration of HIV infection in humans is provided. The vaccine comprises an HIV antigen, esp. a protein which comprises Nef and/or Tat of HIV, and an immunostimulatory **CpG** oligonucleotide. Methods for making the vaccine formulation of the invention are described. Patients may also be treated by pre-administration of the **CpG** oligonucleotide prior to administration of the HIV antigen.

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:12291 CAPLUS
DN 134:99564
TI Vaccines
IN Cohen, Joseph; Garcon, Nathalie; Voss, Gerald
PA Smithkline Beecham Biologicals S.A., Belg.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000231	A2	20010104	WO 2000-EP5841	20000623
	WO 2001000231	A3	20010705		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1198243	A2	20020424	EP 2000-945810	20000623
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
PRAI	GB 1999-15204	A	19990629		
	WO 2000-EP5841	W	20000623		

AB A vaccine formulation for the prevention or amelioration of plasmodium infection in humans is provided. The vaccine comprises a malaria antigen, esp. a protein which comprises a portion of the CS protein of P. falciparum fused in frame via a linear linker to the N-terminal of HBsAg, and an immunostimulatory **CpG** oligonucleotide. Methods for making the vaccine formulation of the invention are described. Patients may also be treated by pre-administration of the **CpG** oligonucleotide prior to administration of the malaria antigen.

L6 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:277876 CAPLUS
DN 132:313678
TI Metal salt particle-adsorbed adjuvant systems and vaccines
IN Garcon, Nathalie
PA Smithkline Beecham Biologicals S. A., Belg.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2000023105 A2 20000427 WO 1999-EP7764 19991008
 WO 2000023105 A3 20000803
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
 CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 BR 9915545 A 20010814 BR 1999-15545 19991008
 EP 1126876 A2 20010829 EP 1999-970607 19991008
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 AU 750587 B2 20020725 AU 2000-11518 19991008
 NZ 511113 A 20020927 NZ 1999-511113 19991008
 JP 2003519084 T2 20030617 JP 2000-576878 19991008
 NO 2001001801 A 20010530 NO 2001-1801 20010409
 ZA 2001002954 A 20020520 ZA 2001-2954 20010410
 PRAI GB 1998-22703 A 19981016
 GB 1998-22709 A 19981016
 GB 1998-22712 A 19981016
 WO 1999-EP7764 W 19991008
 AB The present invention provides vaccine and adjuvant formulations
 comprising an immunostimulant and a metal salt. The immunostimulant is
 adsorbed onto a particle of metal salt (e.g. aluminum hydroxide or
 phosphate) and the resulting particle is essentially devoid of antigen.

=> s l4 and immunomodulatory oligonucleotide
 L7 0 L4 AND IMMUNOMODULATORY OLIGONUCLEOTIDE

=> d his

(FILE 'HOME' ENTERED AT 12:06:12 ON 14 AUG 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
 LIFESCI, CAPLUS' ENTERED AT 12:06:31 ON 14 AUG 2003

E GARCON NATHALIE/AU
 L1 57 S E1-E7
 E COHEN JOSEPH/AU
 L2 119 S E3
 E VOSS GERALD/AU
 L3 73 S E3
 L4 246 S L1-L3
 L5 8 S L4 AND CPG
 L6 8 DUP REM L5 (0 DUPLICATES REMOVED)
 L7 0 S L4 AND IMMUNOMODULATORY OLIGONUCLEOTIDE

=> s l4 and (malaria or plasmodium or rts or trap)
 L8 23 L4 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP)

=> dup rem l8
 PROCESSING COMPLETED FOR L8
 L9 20 DUP REM L8 (3 DUPLICATES REMOVED)

=> d bib ab 1-20

L9 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2003:282425 CAPLUS
 DN 138:302637
 TI Intradermal vaccine compositions comprising saponin, sterol, and LPS

derivative or CpG oligonucleotide as adjuvant

IN **Garcon, Nathalie**
PA Glaxosmithkline Biologicals S.A., Belg.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003028760	A2	20030410	WO 2002-EP10931	20020930
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI GB 2001-23580 A 20011001

AB The present invention provides novel intradermal vaccines and novel uses for adjuvants in the prepn. of intradermal vaccines, and also novel methods of treatment comprising them. The intradermal adjuvants, and methods, of the present invention comprise a saponin and a sterol, wherein the saponin and sterol are formulated in a liposome. The intradermal vaccine further comprises a LPS deriv. or an immunostimulatory CpG oligonucleotide. The intradermal adjuvants are used in the manuf. of intradermal vaccines for humans, and in the intradermal treatment of humans.

L9 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:276663 CAPLUS
DN 138:302632
TI Adjuvant compns. and uses thereof in vaccines
IN Friede, Martin; **Garcon, Nathalie**; Gerard, Catherine Marie
Ghislaine; Hermand, Philippe
PA Smithkline Beecham Biologicals S.A., Belg.
SO U.S., 29 pp., Cont.-in-part of Appl. No. PCT/EP00/02920.
CODEN: USXXAM

DT Patent
LA English

FAN. CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6544518	B1	20030408	US 2000-690921	20001018
	US 6558670	B1	20030506	US 1999-301829	19990429
	WO 2000062800	A2	20001026	WO 2000-EP2920	20000404
	WO 2000062800	A3	20010111		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	WO 2002032450	A2	20020425	WO 2001-EP11984	20011016
	WO 2002032450	A3	20021010		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,			

DN 137:139352
TI Recombinant **Plasmodium** falciparum merozoite protein-142 for use
as diagnostic agent, for antibody production and as vaccine
IN Lyon, Jeffrey A.; Angov, Evelina; Cohen, Joe D.; **Voss, Gerald**
PA Walter Reed Army Institute of Research, USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002058727	A2	20020801	WO 2002-US2554	20020125
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2001-264535P P 20010126

AB Provided is the expression and purifn. of a recombinant **Plasmodium** falciparum (3D7) MSP-142. The method of the present invention produces a highly purified protein which retains folding and disulfide bridging of the native mol. The recombinant MSP-142 is useful as a diagnostic reagent, for use in antibody prodn., and as a vaccine.

L9 ANSWER 5 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 2001:308178 BIOSIS

DN PREV200100308178

TI Hybrid protein between CS from **plasmodium** and HBSAG.

AU De Wilde, Michel (1); **Cohen, Joseph**

CS (1) Glabais Belgium

ASSIGNEE: SmithKline Beecham Biologicals (s.a.), Rixensart, Belgium

PI US 6169171 January 02, 2001

SO Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 2, 2001) Vol. 1242, No. 1, pp. No Pagination. e-file.

ISSN: 0098-1133.

DT Patent

LA English

AB Isolated DNA sequences encoding a novel hybrid protein are provided which comprise a portion of the CS protein of P. falciparum and the surface antigen of Hepatitis B virus. Vectors and host cells containing the isolated DNA sequences are also disclosed.

L9 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2001:12291 CAPLUS

DN 134:99564

TI Vaccines

IN **Cohen, Joseph; Garcon, Nathalie; Voss, Gerald**

PA Smithkline Beecham Biologicals S.A., Belg.

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001000231	A2	20010104	WO 2000-EP5841	20000623
	WO 2001000231	A3	20010705		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,			

SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
 AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6558670 B1 20030506 US 1999-301829 19990429
 BR 2000010612 A 20020213 BR 2000-10612 20000404
 EP 1187629 A2 20020320 EP 2000-920647 20000404

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

JP 2002542203 T2 20021210 JP 2000-611936 20000404
 US 6544518 B1 20030408 US 2000-690921 20001018
 NO 2001005073 A 20011122 NO 2001-5073 20011018

PRAI GB 1999-8885 A 19990419
 US 1999-301829 A 19990429
 WO 2000-EP2920 W 20000404

AB The present invention relates to adjuvant compns. which are suitable to be
 used in vaccines. In particular, the adjuvant compns. of the present
 invention comprises a saponin and an immunostimulatory oligonucleotide,
 optionally with a carrier. Also provided by the present invention are
 vaccines comprising the adjuvants of the present invention and an antigen.
 Further provided are methods of manuf. of the adjuvants and vaccines of
 the present invention and their use as medicaments. Methods of treating
 an individual susceptible to or suffering from a disease by the
 administration of the vaccines of the present invention are also provided.

L9 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:277876 CAPLUS

DN 132:313678

TI Metal salt particle-adsorbed adjuvant systems and vaccines

IN **Garcon, Nathalie**

PA Smithkline Beecham Biologicals S. A., Belg.

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000023105	A2	20000427	WO 1999-EP7764	19991008
	WO 2000023105	A3	20000803		
	W:		AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	BR 9915545	A	20010814	BR 1999-15545	19991008
	EP 1126876	A2	20010829	EP 1999-970607	19991008
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		
	AU 750587	B2	20020725	AU 2000-11518	19991008
	NZ 511113	A	20020927	NZ 1999-511113	19991008
	JP 2003519084	T2	20030617	JP 2000-576878	19991008
	NO 2001001801	A	20010530	NO 2001-1801	20010409
	ZA 2001002954	A	20020520	ZA 2001-2954	20010410
PRAI	GB 1998-22703	A	19981016		
	GB 1998-22709	A	19981016		
	GB 1998-22712	A	19981016		
	WO 1999-EP7764	W	19991008		

AB The present invention provides vaccine and adjuvant formulations comprising an immunostimulant and a metal salt. The immunostimulant is adsorbed onto a particle of metal salt (e.g. aluminum hydroxide or phosphate) and the resulting particle is essentially devoid of antigen.

L9 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:116922 CAPLUS

DN 132:171114

TI Vaccine ISCOM adjuvant using saponin as sole detergent

IN Friede, Martin; **Garcon, Nathalie**

PA Smithkline Beecham Biologicals S.A., Belg.

SO PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000007621	A2	20000217	WO 1999-EP5587	19990803
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2339486	AA	20000217	CA 1999-2339486	19990803
	AU 9955099	A1	20000228	AU 1999-55099	19990803
	AU 738965	B2	20011004		
	EP 1102600	A2	20010530	EP 1999-941506	19990803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002522397	T2	20020723	JP 2000-563304	19990803
	US 6506386	B1	20030114	US 2001-744800	20010604
PRAI	GB 1998-17052	A	19980805		
	WO 1999-EP5587	W	19990803		

AB The present invention provides an improved adjuvant formulation and a process for producing said adjuvant. The adjuvant comprises an ISCOM structure comprising a saponin, said ISCOM structure being devoid of addnl. detergent.

L9 ANSWER 12 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1999:451580 BIOSIS

DN PREV199900451580

TI Hybrid protein between CS from **plasmodium** and HBsAg.

AU De Wilde, Michel (1); **Cohen, Joseph**

CS (1) Glabais Belgium

ASSIGNEE: SmithKline Beecham Biologicals (s.a.)

PI US 5928902 Jul. 27, 1999

SO Official Gazette of the United States Patent and Trademark Office Patents, (Jul. 27, 1999) Vol. 1224, No. 4, pp. NO PAGINATION.

ISSN: 0098-1133.

DT Patent

LA English

L9 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:194018 CAPLUS

DN 130:227707

TI Vaccine adjuvant emulsions containing oils, saponins, and sterols and immunomodulators

IN **Garcon, Nathalie**; Momin, Patricia Marie Christine Aline Françoise

PA Smithkline Beecham Biologicals S.A., Belg.

SO PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9912565	A1	19990318	WO 1998-EP5714	19980902
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2302637	AA	19990318	CA 1998-2302637	19980902
	AU 9896238	A1	19990329	AU 1998-96238	19980902
	EP 1009430	A1	20000621	EP 1998-950005	19980902
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 2001515870	T2	20010925	JP 2000-510462	19980902
	US 6372227	B1	20020416	US 2000-486996	20000424
	US 2002058047	A1	20020516		
PRAI	GB 1997-18901	A	19970905		
	WO 1998-EP5714	W	19980902		

AB The present invention relates to an oil-in-water emulsion compns., their use in medicine, in particular to their use in augmenting immune responses to a wide range of antigens, and to methods of their manuf. The emulsion comprises a metabolizable oil, a saponin, and a sterol. For example, an emulsion was formulated contg. squalene 5, .alpha.-tocopherol 5, Tween-80 2, and water to 100 %. An adjuvant contained 3D-MPL (immunomodulator) 50, QS21 50, the above emulsion 250, phosphate-buffered soln. 250 .mu.L, and cholesterol 500 .mu.g.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:184116 CAPLUS
DN 130:213605
TI Oil-in-water emulsions containing saponins
IN **Garcon, Nathalie**; Momin, Patricia Marie Christine Aline Francoise
PA SmithKline Beecham Biologicals S.A., Belg.
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911241	A1	19990311	WO 1998-EP5715	19980902
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2302554	AA	19990311	CA 1998-2302554	19980902
	AU 9911456	A1	19990322	AU 1999-11456	19980902
	EP 1009382	A1	20000621	EP 1998-954264	19980902
	EP 1009382	B1	20030618		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 2001514208	T2	20010911	JP 2000-508344	19980902
	EP 1279401	A1	20030129	EP 2002-18002	19980902
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9856414	A1	19981217	WO 1998-EP3479	19980603
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9883365	A1	19981230	AU 1998-83365	19980603
	AU 728759	B2	20010118		
	EP 999852	A1	20000517	EP 1998-933600	19980603
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
	BR 9810614	A	20000912	BR 1998-10614	19980603
	JP 2002504106	T2	20020205	JP 1999-501588	19980603
	ZA 9804969	A	19991209	ZA 1998-4969	19980609
	MX 9911439	A	20000630	MX 1999-11439	19991209
	NO 9906133	A	20000126	NO 1999-6133	19991210
PRAI	GB 1997-11990	A	19970611		
	WO 1998-EP3479	W	19980603		

AB The present invention relates to improved stable oil-in-water emulsions having an oil droplet diam. of substantially 300-600 nm comprising triglycerides, and their use as vaccine adjuvants.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:239123 CAPLUS

DN 128:307514

TI Vaccines for infections and cancers

IN **Garcon, Nathalie**; Friede, Martin

PA Smithkline Beecham Biologicals S.A., Belg.; Garcon, Nathalie; Friede, Martin

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9815287	A1	19980416	WO 1997-EP5578	19970930
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9747812	A1	19980505	AU 1997-47812	19970930
	AU 714930	B2	20000113		
	BR 9711853	A	19990824	BR 1997-11853	19970930
	EP 939650	A1	19990908	EP 1997-910430	19970930
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
	CN 1238696	A	19991215	CN 1997-180166	19970930
	NZ 334734	A	20000526	NZ 1997-334734	19970930

JP 2001501640	T2	20010206	JP 1998-517196	19970930
ZA 9708868	A	19990406	ZA 1997-8868	19971003
NO 9901524	A	19990329	NO 1999-1524	19990329
KR 2000048866	A	20000725	KR 1999-702874	19990402
US 2001053365	A1	20011220	US 2001-819464	20010328
PRAI GB 1996-20795	A	19961005		
GB 1995-8326	A	19950425		
EP 1996-910019	A	19960401		
WO 1996-EP1464	W	19960401		
WO 1997-EP5578	W	19970930		
US 1997-945450	B2	19971212		
US 1999-269383	W	19990402		

AB The invention relates to a vaccine compn. comprising an antigen and an adjuvant compn. for treating infections or cancer. The adjuvant compn. comprises alum, an immunol. active saponin fraction (e.g. QS21) assocd. with liposome contg. a phospholipid and a sterol (e.g. cholesterol), and 3-de-O-acylated monophosphoryl lipid A. The antigen is derived from human immunodeficiency virus, feline immunodeficiency virus, varicella zoster virus, herpes simplex virus type 1 and 2, human cytomegalovirus, hepatitis A, B, C or E, respiratory syncytial virus, human papilloma virus, influenza virus, Hib, meningitis virus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, **Plasmodium**, Toxoplasma, or cancer.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:112254 CAPLUS
DN 128:191572
TI Vaccine composition against **malaria**
IN **Cohen, Joseph**
PA Smithkline Beecham Biologicals S.A., Belg.; Cohen, Joseph
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805355	A1	19980212	WO 1997-EP4326	19970731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9742040	A1	19980225	AU 1997-42040	19970731
AU 706303	B2	19990610		
ZA 9706815	A	19980511	ZA 1997-6815	19970731
BR 9710913	A	19990817	BR 1997-10913	19970731
CN 1231613	A	19991013	CN 1997-198360	19970731
EP 957933	A1	19991124	EP 1997-940062	19970731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
JP 2000517295	T2	20001226	JP 1998-507631	19970731
SK 282438	B6	20020205	SK 1999-115	19970731
IL 128318	A1	20020421	IL 1997-128318	19970731
CZ 290826	B6	20021016	CZ 1999-292	19970731
NO 9900464	A	19990201	NO 1999-464	19990201
BG 63290	B1	20010928	BG 1999-103141	19990202
US 2002172692	A1	20021121	US 2001-24860	20011218
US 2003133944	A1	20030717	US 2002-299619	20021118

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9310152	A1	19930527	WO 1992-EP2591	19921111
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	AU 9229278	A1	19930615	AU 1992-29278	19921111
	EP 614465	A1	19940914	EP 1992-923486	19921111
	EP 614465	B1	19990317		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	JP 07501213	T2	19950209	JP 1992-508957	19921111
	AT 177755	E	19990415	AT 1992-923486	19921111
	ES 2129461	T3	19990616	ES 1992-923486	19921111
	CA 2123612	C	20020625	CA 1992-2123612	19921111
	ZA 9208770	A	19940513	ZA 1992-8770	19921113
	US 5928902	A	19990727	US 1996-760797	19961204
	AU 9714717	A1	19970612	AU 1997-14717	19970214
	AU 712409	B2	19991104		
	US 6169171	B1	20010102	US 1997-932929	19970918
	HK 1012405	A1	20000505	HK 1998-113572	19981216
PRAI	GB 1991-24390	A	19911116		
	US 1992-842694	A	19920227		
	WO 1992-EP2591	A	19921111		
	US 1995-442612	B1	19950517		
	US 1996-663371	B1	19960613		

AB Hybrid proteins (**RTS** and **RTS***) are disclosed which include a portion of the CS protein of *P. falciparum* and of the surface antigen of hepatitis B virus (HBsAg). The **RTS** hybrid consists of (1) a Met residue derived from the *Saccharomyces cerevisiae* TDH3 gene sequence; (2) a Met-Ala-Pro sequence; (3) a *P. falciparum* CS protein fragment; (4) an Arg residue; (5) a carboxyl-terminal tetrapeptide sequence (Pro-Val-Thr-Asn) of hepatitis B pre-S2 protein; and (6) hepatitis B S-protein sequence. Also disclosed is a mixed multimeric lipoprotein particle contg. the hybrid protein and HBsAg. The hybrid proteins and particles are useful for anti-malaria vaccines. Expression cassette construction is described, and amino acid sequences (and corresponding nucleotide sequences) are included. (**RTS**,S) lipoprotein particles induced, both in mice and monkeys, a high antibody response directed against the repeat and nonrepeat CS epitopes and against the S protein of the HBsAg carrier. The antibodies elicited in the 2 animal species effectively prevented invasion of cultured human hepatoma cells by *P. falciparum* sporozoites.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	101.39	101.60

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.32	-14.32

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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Aug 8, 2003 (20030808/UP).

=> file biosis medline agricola embase caba wpids japio biotechds lifesci caplus	SINCE FILE	TOTAL
COST IN U.S. DOLLARS		

	ENTRY	SESSION
FULL ESTIMATED COST	0.12	101.72
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
	0.00	-14.32

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 COPYRIGHT (C) 2003 Japanese Patent Office (JPO)- JAPIO

FILE 'BIOTECHDS' ENTERED AT 12:13:03 ON 14 AUG 2003
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FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
 LIFESCI, CAPLUS' ENTERED AT 12:06:31 ON 14 AUG 2003

E GARCON NATHALIE/AU
 L1 57 S E1-E7
 E COHEN JOSEPH/AU
 L2 119 S E3
 E VOSS GERALD/AU
 L3 73 S E3
 L4 246 S L1-L3
 L5 8 S L4 AND CPG
 L6 8 DUP REM L5 (0 DUPLICATES REMOVED)
 L7 0 S L4 AND IMMUNOMODULATORY OLIGONUCLEOTIDE
 L8 23 S L4 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP)
 L9 20 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:11:57 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
 LIFESCI, CAPLUS' ENTERED AT 12:13:03 ON 14 AUG 2003

=> s immunomodulatory (5a) oligonucleotid?

L10 64 IMMUNOMODULATORY (5A) OLIGONUCLEOTID?

=> s l10 and cpg

L11 31 L10 AND CPG

=> s l11 and (plasmodium or malaria or rts or trap)

L12 2 L11 AND (PLASMODIUM OR MALARIA OR RTS OR TRAP)

=> d bib ab 1-2

L12 ANSWER 1 OF 2 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-430170 [40] WPIDS

DNC C2003-113601

TI Composition useful for treating diseases due to pathogens e.g. HIV, or varicella zoster virus, comprises a saponin and a sterol formulated in a liposome.

DC B01 B04

IN GARCON, N

PA (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA

CYC 100

PI WO 2003028760 A2 20030410 (200340)* EN 14p

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW

ADT WO 2003028760 A2 WO 2002-EP10931 20020930

PRAI GB 2001-23580 20011001

AB WO2003028760 A UPAB: 20030624

NOVELTY - A pharmaceutical composition comprises a saponin and a sterol formulated in a liposome.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of a liposome comprising a saponin, a sterol, and an antigen or antigenic preparation in the manufacture of an intradermal vaccine.

ACTIVITY - Antibacterial; Anti-HIV; Hepatotropic; Virucide; Protozoacide; Cytostatic; Nootropic; Neuroprotective; Antiallergic; Antiarteriosclerotic; Antimicrobial.

MECHANISM OF ACTION - Vaccine. The immunogenicity of the respiratory Syncytial virus (RSV) split antigen was evaluated by intradermally administering a preparation containing F protein (4.2 micro g) adjuvanted with QS21 (5 micro g), cholesterol (25 micro g), phosphatidyl choline and 3D-monophosphoryl lipid (5 micro g) to Hartley guinea pigs. The immune response was approx. 100/2300 after 21/14 days respectively.

USE - For treating diseases due to pathogens e.g. HIV, Varicella Zoster virus, Herpes simplex virus type 1 and 2, human cytomegalovirus, Dengue virus, hepatitis A, B, C and E, respiratory syncytical virus, human papilloma virus, influenza virus, Hemophilus influenzae, Meningococcus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, Streptococcus, Mycoplasma, Mycobacteria, **Plasmodium** and Toxoplasma(all claimed). Also for treating cancer, allergy and other infectious diseases, atherosclerosis, and Alzheimer's disease.

ADVANTAGE - The composition requires less amount of antigen and/or saponin adjuvant and thus reduces the associated reactogenic responses. Dwg.0/2

L12 ANSWER 2 OF 2 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2000-524416 [47] WPIDS

CR 1997-145245 [13]; 1997-319766 [29]; 1998-101069 [09]; 1998-609243 [51];
1999-263358 [22]; 1999-313351 [26]; 2000-587434 [55]; 2000-594650 [56];
2001-050094 [06]; 2002-083006 [11]; 2002-393965 [42]; 2003-182286 [18]

DNC C2000-155775

TI Novel methods for obtaining polynucleotides with optimized immunomodulatory responses by directed evolution.

DC B04 C06 D16

IN SHORT, J M

PA (DIVE-N) DIVERSA CORP

CYC 90

PI WO 2000046344 A2 20000810 (200047)* EN 716p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000034839 A 20000825 (200059)

EP 1073710 A2 20010207 (200109) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

ADT WO 2000046344 A2 WO 2000-US3086 20000204; AU 2000034839 A AU 2000-34839
20000204; EP 1073710 A2 EP 2000-913378 20000204, WO 2000-US3086 20000204

FDT AU 2000034839 A Based on WO 200046344; EP 1073710 A2 Based on WO 200046344

PRAI US 1999-246178 19990204

AB WO 200046344 A UPAB: 20030324

NOVELTY - Obtaining a polynucleotide (I) with an optimized immunomodulatory response, or that encodes a polypeptide with an optimized immunomodulatory response comprising creating a library of non-stochastically generated polynucleotides optimized by at least 1 directed evolution method, especially gene saturation mutagenesis and synthetic ligation polynucleotide reassembly, is new.

DETAILED DESCRIPTION - Novel method for obtaining an polynucleotide with an optimized immunomodulatory response, or that encodes a polypeptide with an optimized immunomodulatory response comprising creating a library of non-stochastically generated polynucleotides optimized by at least 1 directed evolution method including the introduction of mutations by non-stochastic methods (especially gene saturation mutagenesis) and by non-stochastic polynucleotide reassembly methods (especially synthetic ligation polynucleotide reassembly).

INDEPENDENT CLAIMS are also included for the following:

- (1) obtaining a polynucleotide as in (I) comprising screening a library of non-stochastically generated polynucleotides and identifying a polynucleotide that has or encodes a polynucleotide with an optimized modulatory effect on an immune response;
- (2) obtaining a polypeptide as in (I) comprising:
 - (a) creating a library of non-stochastically generated polynucleotides; and
 - (b) screening the library to identify a polynucleotide as in (I);
- (3) obtaining an optimized polynucleotide that encodes an accessory molecule that improves the transport or presentation of antigens by a cell, comprising screening a library of non-stochastically generated polynucleotides optimized (for a human or animal) by directed evolution as in (I), for a polynucleotide that encodes a recombinant molecule that modulates antigen transport or presentation;
- (4) obtaining an immunomodulatory polynucleotide with optimized expression in a host comprising creating an optimized non-stochastically generated polynucleotide library as in (I);
- (5) obtaining an immunomodulatory polynucleotide with optimized expression in a host comprising creating and optionally screening a library an optimized non-stochastically generated polynucleotide library;
- (6) producing a progeny polynucleotide set comprising:
 - (a) annealing 2 primers to a circular parental polynucleotide, where the annealment regions of the polynucleotides are non-overlapping and 1 of the primers contains a non-stochastic mutagenic (optionally degenerate) cassette; and
 - (b) synthesizing a progeny polynucleotide for each primer by a

polymerase-catalyzed amplification reaction, where the progeny polynucleotides may form a double-stranded mutagenized circular polynucleotide;

(7) producing progeny polypeptides containing a non-stochastic range of single amino acid substitutions from a template polypeptide, and optionally identifying desirable amino acid substitutions and combinations, comprising:

(a) amplifying a codon-containing template polynucleotide using a degenerate oligonucleotide for each codon to be mutated, where each oligonucleotide comprises a homologous sequence and (at least 1) degenerate trinucleotide cassette;

(b) subjecting the resultant progeny polynucleotides to clonal amplification to express the encoded polypeptides; and optionally

(c) screening the progeny to identify those with a desirable change in at least 1 molecular property compared to the parent polynucleotide.

USE - The methods are useful for obtaining polynucleotide and polypeptides that can be used as genetic vaccines in the immunomodulation of humans and animals. The polynucleotides and peptides are preferably used as vaccines in the treatment, prevention or diagnosis of **malaria**. The methods are also useful for producing polynucleotides and/or polypeptides with enhanced (biological) properties, e.g. increased stability ex vivo (for increased shelf-life and ease of storage), stability in vivo (increased resistance to digestive acids and increased stability in circulation) (claimed), thermostable enzymes, improved vector transfer efficiency, improved immunogenicity, host (e.g. human) optimized vaccine (claimed) and targeted sequences.

Dwg.0/42

=> s l11 and antigen

L13 12 L11 AND ANTIGEN

=> dup rem l13

PROCESSING COMPLETED FOR L13

L14 7 DUP REM L13 (5 DUPLICATES REMOVED)

=> d bib ab 1-7

L14 ANSWER 1 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-430170 [40] WPIDS

DNC C2003-113601

TI Composition useful for treating diseases due to pathogens e.g. HIV, or varicella zoster virus, comprises a saponin and a sterol formulated in a liposome.

DC B01 B04

IN GARCON, N

PA (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA

CYC 100

PI WO 2003028760 A2 20030410 (200340)* EN 14p

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW

ADT WO 2003028760 A2 WO 2002-EP10931 20020930

PRAI GB 2001-23580 20011001

AB WO2003028760 A UPAB: 20030624

NOVELTY - A pharmaceutical composition comprises a saponin and a sterol formulated in a liposome.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of a liposome comprising a saponin, a sterol, and an **antigen** or

antigenic preparation in the manufacture of an intradermal vaccine.

ACTIVITY - Antibacterial; Anti-HIV; Hepatotropic; Virucide; Protozoacide; Cytostatic; Nootropic; Neuroprotective; Antiallergic; Antiarteriosclerotic; Antimicrobial.

MECHANISM OF ACTION - Vaccine. The immunogenicity of the respiratory Syncytial virus (RSV) split **antigen** was evaluated by intradermally administering a preparation containing F protein (4.2 micro g) adjuvanted with QS21 (5 micro g), cholesterol (25 micro g), phosphatidyl choline and 3D-monophosphoryl lipid (5 micro g) to Hartley guinea pigs. The immune response was approx. 100/2300 after 21/14 days respectively.

USE - For treating diseases due to pathogens e.g. HIV, Varicella Zoster virus, Herpes simplex virus type 1 and 2, human cytomegalovirus, Dengue virus, hepatitis A, B, C and E, respiratory syncytical virus, human papilloma virus, influenza virus, Hemophilus influenzae, Meningococcus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, Streptococcus, Mycoplasma, Mycobacteria, Plasmodium and Toxoplasma(all claimed). Also for treating cancer, allergy and other infectious diseases, atherosclerosis, and Alzheimer's disease.

ADVANTAGE - The composition requires less amount of **antigen** and/or saponin adjuvant and thus reduces the associated reactogenic responses.

Dwg.0/2

L14 ANSWER 2 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-354564 [33] WPIDS

DNC C2003-093465

TI New compositions comprising immunostimulatory substances packaged into virus-like particles, useful as a vaccine for enhancing an immune response in animals, e.g. for treating or preventing allergies, tumors or viral infections.

DC B04 D16

IN BACHMANN, M; CIELENS, I; LIPOWSKY, G; MAURER, P; MEIJERINK, E; PUMPENS, P; RENHOFA, R; SCHWARZ, K; STORNI, T; TISSOT, A; BACHMANN, M F

PA (CIEL-I) CIELENS I; (CYTO-N) CYTOS BIOTECHNOLOGY AG; (LIPO-I) LIPOWSKY G; (MAUR-I) MAURER P; (MEIJ-I) MEIJERINK E; (PUMP-I) PUMPENS P; (RENH-I) RENHOFA R; (SCHW-I) SCHWARZ K; (TISS-I) TISSOT A

CYC 101

PI WO 2003024481 A2 20030327 (200333)* EN 322p

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2003099668 A1 20030529 (200337)

ADT WO 2003024481 A2 WO 2002-IB4132 20020916; US 2003099668 A1 Provisional US 2001-318994P 20010914, Provisional US 2002-374145P 20020422, US 2002-244065 20020916

PRAI US 2002-374145P 20020422; US 2001-318994P 20010914; US 2002-244065 20020916

AB WO2003024481 A UPAB: 20030526

NOVELTY - A composition for enhancing immune response in animal comprising a virus-like particle, and an immunostimulatory substance, is new. The immunostimulatory substance is bound to the virus-particle particle.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) enhancing an immune response in an animal by introducing into the animal the new composition;

(2) producing the composition for enhancing an immune response in an animal;

(3) vaccines comprising the new composition together with a pharmaceutical diluent, carrier or excipient; and

20000204; EP 1073710 A2 EP 2000-913378 20000204, WO 2000-US3086 20000204
FDT AU 2000034839 A Based on WO 200046344; EP 1073710 A2 Based on WO 200046344
PRAI US 1999-246178 19990204
AB WO 200046344 A UPAB: 20030324

NOVELTY - Obtaining a polynucleotide (I) with an optimized immunomodulatory response, or that encodes a polypeptide with an optimized immunomodulatory response comprising creating a library of non-stochastically generated polynucleotides optimized by at least 1 directed evolution method, especially gene saturation mutagenesis and synthetic ligation polynucleotide reassembly, is new.

DETAILED DESCRIPTION - Novel method for obtaining an polynucleotide with an optimized immunomodulatory response, or that encodes a polypeptide with an optimized immunomodulatory response comprising creating a library of non-stochastically generated polynucleotides optimized by at least 1 directed evolution method including the introduction of mutations by non-stochastic methods (especially gene saturation mutagenesis) and by non-stochastic polynucleotide reassembly methods (especially synthetic ligation polynucleotide reassembly).

INDEPENDENT CLAIMS are also included for the following:

(1) obtaining a polynucleotide as in (I) comprising screening a library of non-stochastically generated polynucleotides and identifying a polynucleotide that has or encodes a polynucleotide with an optimized modulatory effect on an immune response;

(2) obtaining a polypeptide as in (I) comprising:

(a) creating a library of non-stochastically generated polynucleotides; and

(b) screening the library to identify a polynucleotide as in (I);

(3) obtaining an optimized polynucleotide that encodes an accessory molecule that improves the transport or presentation of antigens by a cell, comprising screening a library of non-stochastically generated polynucleotides optimized (for a human or animal) by directed evolution as in (I), for a polynucleotide that encodes a recombinant molecule that modulates **antigen** transport or presentation;

(4) obtaining an immunomodulatory polynucleotide with optimized expression in a host comprising creating an optimized non-stochastically generated polynucleotide library as in (I);

(5) obtaining an immunomodulatory polynucleotide with optimized expression in a host comprising creating and optionally screening a library an optimized non-stochastically generated polynucleotide library;

(6) producing a progeny polynucleotide set comprising:

(a) annealing 2 primers to a circular parental polynucleotide, where the annealment regions of the polynucleotides are non-overlapping and 1 of the primers contains a non-stochastic mutagenic (optionally degenerate) cassette; and

(b) synthesizing a progeny polynucleotide for each primer by a polymerase-catalyzed amplification reaction, where the progeny polynucleotides may form a double-stranded mutagenized circular polynucleotide;

(7) producing progeny polypeptides containing a non-stochastic range of single amino acid substitutions from a template polypeptide, and optionally identifying desirable amino acid substitutions and combinations, comprising:

(a) amplifying a codon-containing template polynucleotide using a degenerate oligonucleotide for each codon to be mutated, where each oligonucleotide comprises a homologous sequence and (at least 1) degenerate trinucleotide cassette;

(b) subjecting the resultant progeny polynucleotides to clonal amplification to express the encoded polypeptides; and optionally

(c) screening the progeny to identify those with a desirable change in at least 1 molecular property compared to the parent polynucleotide.

USE - The methods are useful for obtaining polynucleotide and polypeptides that can be used as genetic vaccines in the immunomodulation of humans and animals. The polynucleotides and peptides are preferably

used as vaccines in the treatment, prevention or diagnosis of malaria. The methods are also useful for producing polynucleotides and/or polypeptides with enhanced (biological) properties, e.g. increased stability ex vivo (for increased shelf-life and ease of storage), stability in vivo (increased resistance to digestive acids and increased stability in circulation) (claimed), thermostable enzymes, improved vector transfer efficiency, improved immunogenicity, host (e.g. human) optimized vaccine (claimed) and targeted sequences.

Dwg.0/42

L14 ANSWER 6 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 2
 AN 1999-405485 [34] WPIDS
 CR 1999-405369 [34]
 DNC C1999-119781
 TI Composition comprising an E6, E7 or E6/E7 fusion protein from HPV to induce immune response to HPV.
 DC B04 D16
 IN DALEMANS, W L J; GERARD, C M G
 PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
 CYC 86
 PI WO 9933868 A2 19990708 (199934)* EN 62p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
 GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 UA UG US UZ VN YU ZW
 AU 9924191 A 19990719 (199951)
 ZA 9811848 A 20000726 (200042) 63p
 EP 1040123 A2 20001004 (200050) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
 BR 9814487 A 20001010 (200055)
 CZ 2000002376 A3 20001115 (200064)
 AU 729336 B 20010201 (200112)
 HU 2001000526 A2 20010628 (200143)
 JP 2001527091 W 20011225 (200204) 93p
 NZ 505108 A 20021025 (200274)
 ADT WO 9933868 A2 WO 1998-EP8563 19981218; AU 9924191 A AU 1999-24191
 19981218; ZA 9811848 A ZA 1998-11848 19981223; EP 1040123 A2 EP
 1998-966706 19981218, WO 1998-EP8563 19981218; BR 9814487 A BR 1998-14487
 19981218, WO 1998-EP8563 19981218; CZ 2000002376 A3 WO 1998-EP8563
 19981218, CZ 2000-2376 19981218; AU 729336 B AU 1999-24191 19981218; HU
 2001000526 A2 WO 1998-EP8563 19981218, HU 2001-526 19981218; JP 2001527091
 W WO 1998-EP8563 19981218, JP 2000-526542 19981218; NZ 505108 A NZ
 1998-505108 19981218, WO 1998-EP8563 19981218
 FDT AU 9924191 A Based on WO 9933868; EP 1040123 A2 Based on WO 9933868; BR
 9814487 A Based on WO 9933868; CZ 2000002376 A3 Based on WO 9933868; AU
 729336 B Previous Publ. AU 9924191, Based on WO 9933868; HU 2001000526 A2
 Based on WO 9933868; JP 2001527091 W Based on WO 9933868; NZ 505108 A
 Based on WO 9933868
 PRAI GB 1997-27262 19971224
 AB WO 9933868 A UPAB: 20021118
 NOVELTY - A composition (I) comprising an E6 or E7 protein or E6/E7 fusion
 protein from HPV optionally linked to an immunological fusion partner, and
 an **immunomodulatory CpG oligonucleotide**.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:
 (1) a method of inducing an immune response in a patient to an HPV
antigen comprising administering a safe and effective amount of
 (I);
 (2) a method of treating or preventing HPV induced tumors comprising
 administering a safe and effective amount of (I); and
 (3) a method of preparing (I), comprising admixing an E6, E7 or E6/E7

FILE 'CABA' ENTERED AT 12:15:56 ON 14 AUG 2003
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FILE 'WPIDS' ENTERED AT 12:15:56 ON 14 AUG 2003
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FILE 'JAPIO' ENTERED AT 12:15:56 ON 14 AUG 2003
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FILE 'BIOTECHDS' ENTERED AT 12:15:56 ON 14 AUG 2003
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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=> d his

(FILE 'HOME' ENTERED AT 12:06:12 ON 14 AUG 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
LIFESCI, CAPLUS' ENTERED AT 12:06:31 ON 14 AUG 2003

E GARCON NATHALIE/AU

L1 57 S E1-E7

E COHEN JOSEPH/AU

L2 119 S E3

E VOSS GERALD/AU

L3 73 S E3

L4 246 S L1-L3

L5 8 S L4 AND CPG

L6 8 DUP REM L5 (0 DUPLICATES REMOVED)

L7 0 S L4 AND IMMUNOMODULATORY OLIGONUCLEOTIDE

L8 23 S L4 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP)

L9 20 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:11:57 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
LIFESCI, CAPLUS' ENTERED AT 12:13:03 ON 14 AUG 2003

L10 64 S IMMUNOMODULATORY (5A) OLIGONUCLEOTID?

L11 31 S L10 AND CPG

L12 2 S L11 AND (PLASMODIUM OR MALARIA OR RTS OR TRAP)

L13 12 S L11 AND ANTIGEN

L14 7 DUP REM L13 (5 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:15:39 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
LIFESCI, CAPLUS' ENTERED AT 12:15:56 ON 14 AUG 2003

=> dup rem l11

PROCESSING COMPLETED FOR L11

L15 19 DUP REM L11 (12 DUPLICATES REMOVED)

=> d bib ab 1-19

L15 ANSWER 1 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-430170 [40] WPIDS
DNC C2003-113601
TI Composition useful for treating diseases due to pathogens e.g. HIV, or varicella zoster virus, comprises a saponin and a sterol formulated in a liposome.
DC B01 B04
IN GARCON, N
PA (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA
CYC 100
PI WO 2003028760 A2 20030410 (200340)* EN 14p
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW
ADT WO 2003028760 A2 WO 2002-EP10931 20020930
PRAI GB 2001-23580 20011001
AB WO2003028760 A UPAB: 20030624
NOVELTY - A pharmaceutical composition comprises a saponin and a sterol formulated in a liposome.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of a liposome comprising a saponin, a sterol, and an antigen or antigenic preparation in the manufacture of an intradermal vaccine.
ACTIVITY - Antibacterial; Anti-HIV; Hepatotropic; Virucide; Protozoacide; Cytostatic; Nootropic; Neuroprotective; Antiallergic; Antiarteriosclerotic; Antimicrobial.
MECHANISM OF ACTION - Vaccine. The immunogenicity of the respiratory Syncytial virus (RSV) split antigen was evaluated by intradermally administering a preparation containing F protein (4.2 micro g) adjuvanted with QS21 (5 micro g), cholesterol (25 micro g), phosphatidyl choline and 3D-monophosphoryl lipid (5 micro g) to Hartley guinea pigs. The immune response was approx. 100/2300 after 21/14 days respectively.
USE - For treating diseases due to pathogens e.g. HIV, Varicella Zoster virus, Herpes simplex virus type 1 and 2, human cytomegalovirus, Dengue virus, hepatitis A, B, C and E, respiratory syncytial virus, human papilloma virus, influenza virus, Hemophilus influenzae, Meningococcus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, Streptococcus, Mycoplasma, Mycobacteria, Plasmodium and Toxoplasma(all claimed). Also for treating cancer, allergy and other infectious diseases, atherosclerosis, and Alzheimer's disease.
ADVANTAGE - The composition requires less amount of antigen and/or saponin adjuvant and thus reduces the associated reactogenic responses.
Dwg.0/2

L15 ANSWER 2 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STM
AN 2003-354564 [33] WPIDS
DNC C2003-093465
TI New compositions comprising immunostimulatory substances packaged into virus-like particles, useful as a vaccine for enhancing an immune response in animals, e.g. for treating or preventing allergies, tumors or viral infections.
DC B04 D16
IN BACHMANN, M; CIELENS, I; LIPOWSKY, G; MAURER, P; MEIJERINK, E; PUMPENS, P; RENHOFA, R; SCHWARZ, K; STORNI, T; TISSOT, A; BACHMANN, M F
PA (CIEL-I) CIELENS I; (CYTO-N) CYTOS BIOTECHNOLOGY AG; (LIPO-I) LIPOWSKY G; (MAUR-I) MAURER P; (MEIJ-I) MEIJERINK E; (PUMP-I) PUMPENS P; (RENH-I) RENHOFA R; (SCHW-I) SCHWARZ K; (TISS-I) TISSOT A
CYC 101
PI WO 2003024481 A2 20030327 (200333)* EN 322p
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
ZM ZW

US 2003099668 A1 20030529 (200337)

ADT WO 2003024481 A2 WO 2002-IB4132 20020916; US 2003099668 A1 Provisional US
2001-318994P 20010914, Provisional US 2002-374145P 20020422, US
2002-244065 20020916

PRAI US 2002-374145P 20020422; US 2001-318994P 20010914; US 2002-244065
20020916

AB WO2003024481 A UPAB: 20030526

NOVELTY - A composition for enhancing immune response in animal comprising
a virus-like particle, and an immunostimulatory substance, is new. The
immunostimulatory substance is bound to the virus-particle particle.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) enhancing an immune response in an animal by introducing into the
animal the new composition;

(2) producing the composition for enhancing an immune response in an
animal;

(3) vaccines comprising the new composition together with a
pharmaceutical diluent, carrier or excipient; and

(4) immunizing or treating an animal by:

(a) administering the vaccine to the animal;

(b) priming a T cell response in the animal by administering the
vaccine; or

(c) boosting a T cell response in the animal by administering the
vaccine.

ACTIVITY - Immunostimulant; Cytostatic; Antiallergic; Virucide;
Antibacterial.

Mice were subcutaneously primed with 100 micro g p33-VLP alone, mixed
with 20 nmol **CpG**-oligonucleotide (p33-VLP+**CpG**), or
p33-VLP packaged with **CpG**-oligonucleotide after dialysis of free
CpG-oligonucleotide (p33-VLP/**CpG**). Untreated naive mice
served as negative control. Twenty days later, mice were challenged with
lymphocytic choriomeningitis virus (LCMV) (200 plaque forming units
(pfu)), intravenously). Results showed that LCMV titer (log10) was lowest
for p33-VLP/**CpG**.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful as a vaccine for enhancing an immune
response in an animal, particularly a mammal or human. Specifically, the
composition is useful for enhancing a B cell response, a T cell response
(particularly a Th or Th1 cell response), or a cytotoxic T-lymphocyte
(CTL) response. (All claimed.) The composition or vaccine is also useful
for immunizing or treating an animal (claimed), e.g. humans, sheep,
horses, cattle, pigs, dogs, cats, rats, birds, reptiles or fish. The
composition is particularly useful as prophylactic or therapeutic vaccines
against allergies, tumors (e.g. breast cancers, neuroblastoma, or
leukemia), viral diseases (e.g. influenza, hepatitis, measles or chicken
pox), or bacterial infections (e.g. tuberculosis, pneumonia or syphilis).
Dwg. 0/55

L15 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:532336 CAPLUS

DN 139:79154

TI Use of immunomodulatory **CpG** oligodeoxynucleotides for treatment
of inflammatory bowel disease and other gastrointestinal inflammation

IN Raz, Eyal; Rachmilewitz, Daniel

PA USA

SO U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of U.S. Ser. No. 791,500.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003130217	A1	20030710	US 2002-219143	20020813
	US 2002042387	A1	20020411	US 2001-791500	20010222
PRAI	US 2000-184256P	P	20000223		
	US 2001-791500	A2	20010222		

AB The invention provides a method for ameliorating gastrointestinal inflammation, particularly chronic gastrointestinal inflammation such as inflammatory bowel disease (IBD), in a subject. In one embodiment, the method comprises administering an immunomodulatory nucleic acid to a subject suffering from or susceptible to gastrointestinal inflammation.

L15 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:319450 CAPLUS

DN 138:331689

TI Polarization of the helper T-cell response with immunostimulatory nucleic acid

IN Raz, Eyal; Broide, David

PA USA

SO U.S. Pat. Appl. Publ., 56 pp., Cont.-in-part of U.S. Ser. No. 235,742.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003078223	A1	20030424	US 2002-99512	20020315
	US 6498148	B1	20021224	US 1999-235742	19990121
	AU 759590	B2	20030417	AU 2001-23162	20010221
	US 2003109469	A1	20030612	US 2002-99379	20020614
	US 2003092663	A1	20030515	US 2002-229208	20020826
PRAI	US 1996-593554	B1	19960130		
	US 1997-927120	B2	19970905		
	US 1999-235742	A2	19990121		
	US 1999-265191	A2	19990310		
	US 2001-276865P	P	20010316		
	US 1993-112440	B2	19930826		
	US 1995-446691	B2	19950607		
	AU 1997-18418	A3	19970128		

AB The authors disclose methods of maintaining suppression of a Th2 immune response and increasing a Th1 immune response in an individual. The methods generally involve administering to an individual an effective amt. of an immunostimulatory nucleic acid. In one example, administration of an immunostimulatory oligonucleotide suppresses pulmonary eosinophil accumulation in a Th2-driven model of asthma. Amelioration of the immunol. markers assocd. with asthma pathol. was shown to coincide with polarization to a type 1 helper T-cell response.

L15 ANSWER 5 OF 19 MEDLINE on STN

DUPLICATE 1

AN 2003377262 IN-PROCESS

DN 22793610 PubMed ID: 12912966

TI Protection of Mice against Philadelphia Chromosome-positive Acute Lymphoblastic Leukemia by Cell-based Vaccination Using Nonviral, Minimalistic Expression Vectors and **Immunomodulatory Oligonucleotides**.

AU Kochling Joachim; Konig-Merediz Sven A; Stripecke Renata; Buchwald Dirk; Korte Alexander; Von Einsiedel Hagen G; Sack Florian; Henze Gunter; Seeger Karl; Wittig Burghardt; Schmidt Manuel

CS Department of Pediatric Hematology, Children's Hospital, University of Tübingen, D-72076 Tübingen, Germany [J. K.].

SO CLINICAL CANCER RESEARCH, (2003 Aug) 9 (8) 3142-9.

Journal code: 9502500. ISSN: 1078-0432.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030813
Last Updated on STN: 20030813
AB PURPOSE: Childhood Philadelphia chromosome positive (Ph(+)) acute lymphoblastic leukemia (ALL) has a poor prognosis. Because leukemia cell burden is reduced but not eradicated by polychemotherapy, improved treatment strategies should enhance those immune mechanisms responsible for the maintenance of complete remission. The aim of this study was to evaluate the protection of mice challenged with the syngeneic Ph(+) ALL cell line BM185 using genetically modified leukemia cell vaccines and immunomodulating oligonucleotides. Experimental Design: Because retroviral vectors are ineffective at transducing nondividing primary cells from human hematopoietic malignancies, we first evaluated nonviral techniques (electroporation and ballistic transfer) using minimalistic immunogenically defined gene expression vectors to generate B7.1 or granulocyte macrophage colony-stimulating factor (GM-CSF)-expressing BM185 cells. Subsequently, protective vaccination experiments with these cells were performed in a leukemia challenge mouse model. RESULTS: Electroporation yielded a high transfection rate (82.6% for B7.1) with moderate GM-CSF secretion/1 x 10(6) cells (228 pg), whereas ballistic transfer led to a lower transfection rate (30.9%) with high GM-CSF secretion (614 pg). Secondly, we immunized mice with B7.1/interleukin 2- or B7.1/GM-CSF-expressing BM185 cell vaccines. We observed a better protection of mice that received the B7.1/GM-CSF vaccine compared with those receiving the B7.1/interleukin 2 vaccine. Protection was additionally enhanced by application of a double stem-loop immunomodulating oligonucleotide containing CpG motifs. CONCLUSION: Our data indicate that immunization with B7.1/GM-CSF-expressing cell vaccines generated by electroporation and application of double stem-loop immunomodulating oligonucleotide protected mice against a murine Ph(+) ALL challenge. Ultimately, this approach may also lead to clinical benefit in patients with Ph(+) ALL.

L15 ANSWER 6 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:359746 BIOSIS
DN PREV200300359746
TI Down-regulation of Th2 cytokines in vitro by **immunomodulatory oligonucleotides** (IMO) containing modified **CpG** motifs.
AU Srivastava, K. D. (1); Kandimalla, E. R.; Yu, D.; Agrawal, S.; Sampson, H. A. (1); Li, X. (1)
CS (1) Pediatrics, Mount Sinai School of Medicine, New York, NY, USA USA
SO Journal of Allergy and Clinical Immunology, (February 2003, 2003) Vol. 111, No. 2 Abstract Supplement, pp. S263. print.
Meeting Info.: AAAAI 60th Anniversary Meeting Denver, CO, USA March 07-12, 2003 American Academy of Allergy, Asthma and Immunology
. ISSN: 0091-6749.
DT Conference
LA English

L15 ANSWER 7 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2002:529252 BIOSIS
DN PREV200200529252
TI **CpG** oligodeoxynucleotides induce human monocytes to mature into functional dendritic cells.
AU Gursel, Mayda; Verthelyi, Daniela; Klinman, Dennis M. (1)
CS (1) Section of Retroviral Immunology, Center for Biologics Evaluation and Research, Food and Drug Administration, Bldg 29A Rm 3 D 10, CBER/FDA, Bethesda, MD, 20892: Klinman@CBER.FDA.GOV USA
SO European Journal of Immunology, (September, 2002) Vol. 32, No. 9, pp.

2617-2622. <http://www.wiley-vch.de/publish/en/journals/alphabeticIndex/2040/?sID=87ce709e9d93384f19ebcbf2d13f6116>. print.

ISSN: 0014-2980.

DT Article

LA English

AB Dendritic cells (DC) excel at presenting antigen to T cells and thus make a key contribution to the induction of primary and secondary immune responses. DC matured in vitro and pulsed with antigen show promise for the immunotherapy of cancer and infectious diseases. Synthetic **oligonucleotides** (ODN) expressing **immunomodulatory "CpG motifs"** were found to boost APC function in mice. Current results demonstrate that the recently identified "D" type of **CpG** ODN stimulate human peripheral blood monocytes to mature into functionally active DC over 2-4 days. The transition from monocyte to DC is characterized by the up-regulation of CD83, CD86, CD80, CD40 and the down-regulation of CD14. These DC support antigen-specific humoral and cellular responses in vitro and in vivo. The differentiation of these monocytes is mediated by plasmacytoid DC, which respond to D type ODN by secreting IFN-alpha. Since D type **CpG** motifs are present in bacterial and viral DNA, the maturation of monocytes into functional DC may reflect a physiologic response that can be harnessed therapeutically through the use of **CpG** ODN.

L15 ANSWER 8 OF 19 MEDLINE on STN DUPLICATE 3

AN 2002302825 MEDLINE

DN 22038900 PubMed ID: 12044033

TI Towards optimal design of second-generation **immunomodulatory oligonucleotides**.

AU Kandimalla Ekambar R; Yu Dong; Agrawal Sudhir

CS Hybridon Inc., Cambridge, MA 02139, USA.

SO Curr Opin Mol Ther, (2002 Apr) 4 (2) 122-9. Ref: 58

Journal code: 100891485. ISSN: 1464-8431.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 200211

ED Entered STN: 20020605

Last Updated on STN: 20021211

Entered Medline: 20021119

AB The goal of using of oligodeoxyribonucleotides containing **CpG** dinucleotides (**CpG** DNA) as immunomodulatory agents has been realized in recent years. Therapeutic applications of **CpG** DNA as monotherapies and as adjuvants in combination with vaccines, antibodies, antigens and allergens for a number of disease indications are rapidly expanding, and the safety and efficacy of several first-generation **CpG** DNA agents are being evaluated in human clinical trials. The biological effects of **CpG** DNA have been known for two decades; however, only recently has a specific receptor(s) that recognizes **CpG** DNA and activates immune cascade been identified. A number of sequence and structural characteristics of **CpG** DNA and chemical modifications that influence immunostimulatory activity have been identified. In this article we summarize the recent progress in understanding the structural and chemical characteristics of **CpG** DNA that are significant for molecular recognition. In addition, we describe the design of second-generation **CpG** DNA agents, and clinical applications of first-generation agents.

L15 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:586761 BIOSIS

DN PREV200200586761

TI In vitro immunomodulatory effects of **CpG** motifs as potential vaccine adjuvants.
 AU Xie, H. (1); Raybourne, R.; Babu, U.; Lillehoj, H.; Heckert, R. (1)
 CS (1) VA-MD Regional College of Veterinary Medicine, University of Maryland, College Park, MD USA
 SO Poultry Science, (2002) Vol. 81, No. Supplement 1, pp. 9. print.
 Meeting Info.: 91st Annual Meeting of the Poultry Science Association
 Newark, DE, USA August 08-11, 2002 Southern Poultry Science Society
 . ISSN: 0032-5791.
 DT Conference
 LA English

L15 ANSWER 10 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2001:380103 BIOSIS
 DN PREV200100380103
 TI **Immunomodulatory oligonucleotides.**
 AU Krieg, Arthur M.; Klinman, Dennis (1); Steinberg, Alfred D.
 CS (1) Potomac, MD USA
 ASSIGNEE: The University of Iowa Research Foundation; The United States of America; Coley Pharmaceutical Group, Newark, DE, USA
 PI US 6194388 February 27, 2001
 SO Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4, pp. No Pagination. e-file.
 ISSN: 0098-1133.
 DT Patent
 LA English
 AB Oligonucleotides containing unthylated **CpG** dinucleotides and therapeutic utilities based on their ability to stimulate an immune response in a subject are disclosed. Also disclosed are therapies for treating diseases associated with immune system activation that are initiated by unthylated **CpG** dinucleotides in a subject comprising administering to the subject oligonucleotides that do not contain unmethylated **CpG** sequences (i.e. methylated **CpG** sequences or no **CpG** sequence) to outcompete unmethylated **CpG** nucleic acids for binding. Further disclosed are methylated **CpG** containing dinucleotides for use antisense therapies or as in vivo hybridization probes, and immunoinhibitory oligonucleotides for use as antiviral therapeutics.

L15 ANSWER 11 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 2002-062105 [08] WPIDS
 DNC C2002-017719
 TI Modulating an immunostimulatory effect of a **CpG** dinucleotide containing compound for antisense or immunotherapy applications, comprises introducing an immunomodulatory group at a position either 5' to or 3' to a **CpG** dinucleotide.
 DC B02 B04 D16
 IN AGRAWAL, S; KANDIMALLA, E
 PA (HYBR-N) HYBRIDON INC; (AGRA-I) AGRAWAL S; (KAND-I) KANDIMALLA E
 CYC 92
 PI WO 2001083503 A2 20011108 (200208)* EN 27p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
 FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
 LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
 TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
 AU 2001057366 A 20011112 (200222)
 US 2002132995 A1 20020919 (200264)
 EP 1278761 A2 20030129 (200310) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 ADT WO 2001083503 A2 WO 2001-US13682 20010430; AU 2001057366 A AU 2001-57366

20010430; US 2002132995 A1 Provisional US 2000-201578P 20000501, US
2001-845623 20010430; EP 1278761 A2 EP 2001-930870 20010430, WO
2001-US13682 20010430

FDT AU 2001057366 A Based on WO 200183503; EP 1278761 A2 Based on WO 200183503

PRAI US 2000-201578P 20000501; US 2001-845623 20010430

AB WO 200183503 A UPAB: 20021031

NOVELTY - Modulating (M) the immunostimulatory effect of a **CpG** dinucleotide containing compound, involves introducing an immunomodulatory group at a position either 5' to or 3' to the **CpG** dinucleotide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a compound (I) having increased or reduced immunostimulatory effect, comprising a **CpG** dinucleotide and an immunomodulatory group, where the increased or reduced immunomodulatory effect is relative to a similar compound lacking the immunomodulatory group;

(2) obtaining an antisense-specific reduction in the expression of a gene in a mammal comprising administering an oligonucleotide that is complementary to the gene and which comprises a **CpG** dinucleotide and an **immunomodulatory** group, where the **oligonucleotide** has less immunostimulatory effect than a similar **oligonucleotide** lacking the **immunomodulatory** group; and

(3) inducing an immune response in a mammal comprising administering to the mammal a compound which comprises a **CpG** dinucleotide and an immunomodulatory group, where the compound has greater immunostimulatory effect than a similar compound lacking the immunomodulatory group.

ACTIVITY - Immunostimulant.

MECHANISM OF ACTION - Immunostimulatory effect of a **CpG** dinucleotide containing compound modulator; immune response inducer (claimed). To study the impact of the site of chemical modification of PS-oligos containing a **CpG** motif, two oligonucleotides oligo 1 and oligo 2 were chosen, each of which contained one **CpG** motif. To evaluate the immunostimulatory activity of oligonucleotides, a mouse spleen cell proliferation assay was used. Mouse spleen lymphocytes were cultured with oligonucleotides at concentration of 0.1, 1, and 10 micro g/mL. Oligo 1 and oligo 2 induced a dose dependent effect on cell proliferation. At 0.1 micro g/L, the proliferation index increased. Substitution of 5'-flanking deoxynucleoside (Y1) of **CpG** motif of oligo 1 or oligo 2 with an immunomodulatory group having the structure (S) resulted in complete suppression of cell proliferation at all concentrations used. At 0.1 micro g/mL, cell proliferation index was similar to medium alone. Substitution of the 3'-flanking deoxynucleoside (X1) of **CpG** motif of oligo 1 or oligo 2 with 2'-OMe did not have such an impact on cell proliferation, but reduced it slightly. Similar substitutions were made in oligo 1 or oligo 2 in the 3'-flanking region to **CpG** motif. Oligos were synthesized in which a deoxynucleoside was substituted with an immunomodulatory group at position X3, X4, X5 or X6. The proliferation index of these oligos increased.

5'-Yn...Y6-Y5-Y4-Y3-Y2-Y1-CG-X1-X2-X3-X4-X5-X6-X7-X8-X9...Xm-3'

C = cytosine;

G = guanosine, substituted guanosine, including inosine and 7-deazaguanosine;

each X and Y = a nucleoside or an immunomodulatory group;

n = a number from -9 to +20; and

m = a number from -6 to +20.

USE - (M) is useful for modulating the immunostimulatory effect of a **CpG** dinucleotide containing compound. (I) is useful for obtaining an antisense-specific reduction in the expression of a gene in a mammal, preferably a human, by administering to the mammal an oligonucleotide that is complementary to the gene and which comprises a **CpG** dinucleotide and an **immunomodulatory** group, where the **oligonucleotide** has less immunostimulatory effect than a similar **oligonucleotide** lacking the **immunomodulatory** group. The

oligonucleotide has only one **immunomodulatory** group for each **CpG** dinucleotide present in the oligonucleotide. The oligonucleotide is administered at a sufficient dosage to attain a blood level of oligonucleotide from about 0.01-10 micro molar. (I) is also useful for inducing an immune response in a mammal, by administering (I) to the mammal, where (I) has greater immunostimulatory effect than a similar compound lacking the immunomodulatory group. The method further comprises administering an adjuvant (claimed). (M) is useful for antisense and immunotherapy applications. (M) or (I) is useful in animal models of disease or gene expression, and for the therapeutic treatment of human or animal disease.

Dwg.0/3

L15 ANSWER 12 OF 19 MEDLINE on STN DUPLICATE 4
 AN 2002431977 MEDLINE
 DN 22176504 PubMed ID: 12188879
 TI Antisense and/or immunostimulatory oligonucleotide therapeutics.
 AU Agrawal S; Kandimalla E R
 CS Hybridon, Inc., 345 Vassar Street, Cambridge, MA 02139, USA..
 sagrawal@hybridon.com
 SO Curr Cancer Drug Targets, (2001 Nov) 1 (3) 197-209. Ref: 93
 Journal code: 101094211. ISSN: 1568-0096.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 200210
 ED Entered STN: 20020822
 Last Updated on STN: 20021002
 Entered Medline: 20021001
 AB Antisense technology, which is based on a simple and rational principle of Watson-Crick complementary base pairing of a short oligonucleotide with the targeted mRNA to downregulate the disease-causing gene product, has progressed tremendously in the last two decades. Antisense oligonucleotides targeted to a number of cancer-causing genes are being evaluated in human clinical trials. While the first-generation phosphorothioate antisense oligonucleotides are in clinical trials, a number of factors, including sequence motifs that could lead to unwanted mechanisms of action and side effects, have been identified. The severity of the side effects of first-generation antisense oligonucleotides is mostly dependent on the presence of certain sequence motifs, such as **CpG** dinucleotides. A number of second-generation chemical modifications have been proposed to overcome the limitations of the first-generation antisense oligonucleotides. The safety and efficacy of several second-generation mixed-backbone antisense oligonucleotides are being evaluated in clinical trials. The immune stimulation affects observed with **CpG**-containing antisense oligonucleotides are being exploited as a novel therapeutic modality, with several **CpG** oligonucleotides being evaluated in clinical trials. A number of medicinal chemistry studies performed to date suggest that the **immunomodulatory** activity of **CpG** **oligonucleotides** can be fine-tuned by site-specific incorporation of chemical modifications in order to design disease-specific oligonucleotide therapeutics.

L15 ANSWER 13 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2001:175367 BIOSIS
 DN PREV200100175367
 TI Modulation of eosinophilic inflammation by **CpG** oligodeoxynucleotides in a murine model of rhinosinusitis.
 AU Hussain, Iftikhar (1); Kitagaki, Kunihiro (1); Businga, Thomas (1); Jain,

Vipul (1); Kline, Joel (1)
CS (1) University of Iowa, Iowa City, IA USA
SO Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S150-S151. print.
Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001
ISSN: 0091-6749.
DT Conference
LA English
SL English

L15 ANSWER 14 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-524416 [47] WPIDS
CR 1997-145245 [13]; 1997-319766 [29]; 1998-101069 [09]; 1998-609243 [51]; 1999-263358 [22]; 1999-313351 [26]; 2000-587434 [55]; 2000-594650 [56]; 2001-050094 [06]; 2002-083006 [11]; 2002-393965 [42]; 2003-182286 [18]
DNC C2000-155775
TI Novel methods for obtaining polynucleotides with optimized immunomodulatory responses by directed evolution.
DC B04 C06 D16
IN SHORT, J M
PA (DIVE-N) DIVERSA CORP
CYC 90
PI WO 2000046344 A2 20000810 (200047)* EN 716p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000034839 A 20000825 (200059)
EP 1073710 A2 20010207 (200109) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
ADT WO 2000046344 A2 WO 2000-US3086 20000204; AU 2000034839 A AU 2000-34839 20000204; EP 1073710 A2 EP 2000-913378 20000204, WO 2000-US3086 20000204
FDT AU 2000034839 A Based on WO 200046344; EP 1073710 A2 Based on WO 200046344
PRAI US 1999-246178 19990204
AB WO 200046344 A UPAB: 20030324
NOVELTY - Obtaining a polynucleotide (I) with an optimized immunomodulatory response, or that encodes a polypeptide with an optimized immunomodulatory response comprising creating a library of non-stochastically generated polynucleotides optimized by at least 1 directed evolution method, especially gene saturation mutagenesis and synthetic ligation polynucleotide reassembly, is new.
DETAILED DESCRIPTION - Novel method for obtaining an polynucleotide with an optimized immunomodulatory response, or that encodes a polypeptide with an optimized immunomodulatory response comprising creating a library of non-stochastically generated polynucleotides optimized by at least 1 directed evolution method including the introduction of mutations by non-stochastic methods (especially gene saturation mutagenesis) and by non-stochastic polynucleotide reassembly methods (especially synthetic ligation polynucleotide reassembly).
INDEPENDENT CLAIMS are also included for the following:
(1) obtaining a polynucleotide as in (I) comprising screening a library of non-stochastically generated polynucleotides and identifying a polynucleotide that has or encodes a polynucleotide with an optimized modulatory effect on an immune response;
(2) obtaining a polypeptide as in (I) comprising:
(a) creating a library of non-stochastically generated polynucleotides; and
(b) screening the library to identify a polynucleotide as in (I);
(3) obtaining an optimized polynucleotide that encodes an accessory

L15 ANSWER 16 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 5
 AN 2000:301619 BIOSIS
 DN PREV2000000301619
 TI **Immunomodulatory oligonucleotides.**
 AU Krieg, Arthur M. (1)
 CS (1) Iowa City, IA USA
 ASSIGNEE: University of Iowa Research Foundation, Iowa City, IA, USA
 PI US 6008200 December 28, 1999
 SO Official Gazette of the United States Patent and Trademark Office Patents,
 (Dec. 28, 1999) Vol. 1229, No. 4, pp. No pagination. e-file.
 ISSN: 0098-1133.
 DT Patent
 LA English
 AB Oligonucleotides containing unthylated **CpG** dinucleotides and
 therapeutic utilities based on their ability to stimulate an immune
 response in a subject are disclosed. Also disclosed are therapies for
 treating diseases associated with immune system activation that are
 initiated by unthylated **CpG** dinucleotides in a subject
 comprising administering to the subject oligonucleotides that do not
 contain unmethylated **CpG** sequences (i.e. methylated **CpG**
 sequences or no **CpG** sequence) to outcompete unmethylated
CpG nucleic acids for binding. Further disclosed are methylated
CpG containing dinucleotides for use antisense therapies or as in
 vivo hybridization probes, and immunoinhibitory oligonucleotides for use
 as antiviral therapeutics.

L15 ANSWER 17 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 6
 AN 1999-405485 [34] WPIDS
 CR 1999-405369 [34]
 DNC C1999-119781
 TI Composition comprising an E6, E7 or E6/E7 fusion protein from HPV to
 induce immune response to HPV.
 DC B04 D16
 IN DALEMANS, W L J; GERARD, C M G
 PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
 CYC 86
 PI WO 9933868 A2 19990708 (199934)* EN 62p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
 GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 UA UG US UZ VN YU ZW
 AU 9924191 A 19990719 (199951)
 ZA 9811848 A 20000726 (200042) 63p
 EP 1040123 A2 20001004 (200050) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
 BR 9814487 A 20001010 (200055)
 CZ 2000002376 A3 20001115 (200064)
 AU 729336 B 20010201 (200112)
 HU 2001000526 A2 20010628 (200143)
 JP 2001527091 W 20011225 (200204) 93p
 NZ 505108 A 20021025 (200274)
 ADT WO 9933868 A2 WO 1998-EP8563 19981218; AU 9924191 A AU 1999-24191
 19981218; ZA 9811848 A ZA 1998-11848 19981223; EP 1040123 A2 EP
 1998-966706 19981218, WO 1998-EP8563 19981218; BR 9814487 A BR 1998-14487
 19981218, WO 1998-EP8563 19981218; CZ 2000002376 A3 WO 1998-EP8563
 19981218, CZ 2000-2376 19981218; AU 729336 B AU 1999-24191 19981218; HU
 2001000526 A2 WO 1998-EP8563 19981218, HU 2001-526 19981218; JP 2001527091
 W WO 1998-EP8563 19981218, JP 2000-526542 19981218; NZ 505108 A NZ
 1998-505108 19981218, WO 1998-EP8563 19981218

FDT AU 9924191 A Based on WO 9933868; EP 1040123 A2 Based on WO 9933868; BR 9814487 A Based on WO 9933868; CZ 2000002376 A3 Based on WO 9933868; AU 729336 B Previous Publ. AU 9924191, Based on WO 9933868; HU 2001000526 A2 Based on WO 9933868; JP 2001527091 W Based on WO 9933868; NZ 505108 A Based on WO 9933868

PRAI GB 1997-27262 19971224

AB WO 9933868 A UPAB: 20021118

NOVELTY - A composition (I) comprising an E6 or E7 protein or E6/E7 fusion protein from HPV optionally linked to an immunological fusion partner, and an **immunomodulatory CpG oligonucleotide**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of inducing an immune response in a patient to an HPV antigen comprising administering a safe and effective amount of (I);

(2) a method of treating or preventing HPV induced tumors comprising administering a safe and effective amount of (I); and

(3) a method of preparing (I), comprising admixing an E6, E7 or E6/E7 fusion protein optionally linked to an immunological fusion partner, and an **immunomodulatory CpG oligonucleotide**.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The composition can be used to induce an immune response in a patient to an HPV antigen. It can also be used for preventing or treating HPV induced tumors (all claimed).

ADVANTAGE - None given.

Dwg. 0/6

L15 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1998:158397 BIOSIS

DN PREV199800158397

TI **Immunomodulatory effects of CPG-based oligonucleotides** (OLIGOS) patterned after sequences present in bacterial DNA.

AU Klinman, Dennis M. (1)

CS (1) Cent. Biol., FDA, Bethesda, MD 20892 USA

SO Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S276.

Meeting Info.: 61st National Scientific Meeting of the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.

DT Conference

LA English

L15 ANSWER 19 OF 19 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

AN 1996-05191 BIOTECHDS

TI New **immunomodulatory oligonucleotides**; containing an unmethylated **CpG** dinucleotide for stimulating activity or methylated for inhibitory activity; application in immune deficiency disease therapy and diagnosis

AU Krieg A M

PA Univ.Iowa-Res.Found.

LO Iowa City, IA, USA.

PI WO 9602555 1 Feb 1996

AI WO 1995-US1570 7 Feb 1995

PRAI US 1994-276358 15 Jul 1994

DT Patent

LA English

OS WPI: 1996-105847 [11]

AB An oligonucleotide (ON) is claimed, comprising 2-100 nucleotides and containing at least 1 unmethylated **CpG** dinucleotide. Also claimed are: i. a method for treating a disease associated with an immune system activation which comprises administering a neutral ON alone or in

conjunction with a carrier; ii. an improved method for performing antisense therapy comprising methylating CpG-containing ONs prior to administration; iii. an improved method for in vivo diagnosis using ON probes comprising methylating CpG-containing ONs prior to administration; iv. an ON which is capable of interfering with the activity of viral or cellular transcription factors and containing a consensus immunoinhibitory CpG motif of formula (I) 5'-GCGXnGCG-3', where X = nucleotide, and n = 0-50. 2 Specific ONs are claimed: 5'-GGGGTCAACGTTGAGGGGGG-3' and (I) where Xn is a CpG dinucleotide. The unmethylated CpG-containing ONs can be used to activate B-lymphocytes and natural killer cells (claimed). They can be used for treating, preventing or ameliorating an immune system deficiency (claimed), e.g. a tumor or cancer or a viral, fungal, bacterial or parasitic infection in a subject. (45pp)

```
=> s cpg and adjuvant
L16      1286 CPG AND ADJUVANT
```

```
=> dup rem l16
PROCESSING COMPLETED FOR L16
L17      513 DUP REM L16 (773 DUPLICATES REMOVED)
```

```
=> s l17 and immunostimulat?
L18      216 L17 AND IMMUNOSTIMULAT?
```

```
=> s l18 and (malaria or plasmodium or rts or trap or hybrid)
L19      19 L18 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP OR HYBRID)
```

```
=> d his
```

(FILE 'HOME' ENTERED AT 12:06:12 ON 14 AUG 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 12:06:31 ON 14 AUG 2003

```
      E GARCON NATHALIE/AU
L1      57 S E1-E7
      E COHEN JOSEPH/AU
L2      119 S E3
      E VOSS GERALD/AU
L3      73 S E3
L4      246 S L1-L3
L5      8 S L4 AND CPG
L6      8 DUP REM L5 (0 DUPLICATES REMOVED)
L7      0 S L4 AND IMMUNOMODULATORY OLIGONUCLEOTIDE
L8      23 S L4 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP)
L9      20 DUP REM L8 (3 DUPLICATES REMOVED)
```

FILE 'STNGUIDE' ENTERED AT 12:11:57 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 12:13:03 ON 14 AUG 2003

```
L10     64 S IMMUNOMODULATORY (5A) OLIGONUCLEOTID?
L11     31 S L10 AND CPG
L12     2 S L11 AND (PLASMODIUM OR MALARIA OR RTS OR TRAP)
L13     12 S L11 AND ANTIGEN
L14     7 DUP REM L13 (5 DUPLICATES REMOVED)
```

FILE 'STNGUIDE' ENTERED AT 12:15:39 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 12:15:56 ON 14 AUG 2003

```
L15     19 DUP REM L11 (12 DUPLICATES REMOVED)
```

oil solution, that also contained one of three oligodeoxynucleotides. The animals receiving oligodeoxynucleotides containing either three or four **CpG** motifs produced antibodies that bound a recombinant CSP as measured in ELISA, and reacted with *P. falciparum* sporozoites in a sporozoite immunofluorescent test. These responses were significantly greater than those seen in animals receiving the oligodeoxynucleotide without **CpG** motifs. These data indicate that oligodeoxynucleotides containing **CpG** motifs improve immunogenicity of peptide immunogens in non-human primates, and may be immunopotentiators useful in humans.

L19 ANSWER 3 OF 19 MEDLINE on STN
 AN 2001678559 MEDLINE
 DN 21571712 PubMed ID: 11714813
 TI Efficient delivery of Antennapedia homeodomain fused to CTL epitope with liposomes into dendritic cells results in the activation of CD8+ T cells.
 AU Chikh G G; Kong S; Bally M B; Meunier J C; Schutze-Redelmeier M P
 CS Systemic Therapy Program, Department of Advanced Therapeutics, British Columbia Cancer Research Centre, Vancouver, British Columbia, Canada.
 SO JOURNAL OF IMMUNOLOGY, (2001 Dec 1) 167 (11) 6462-70.
 Journal code: 2985117R. ISSN: 0022-1767.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 200201
 ED Entered STN: 20011129
 Last Updated on STN: 20020124
 Entered Medline: 20020102
 AB The in vivo induction of a CTL response using Antennapedia homeodomain (AntpHD) fused to a poorly immunogenic CTL epitope requires that the Ag is given in presence of SDS, an unacceptable **adjuvant** for human use. In the present report, we developed a **hybrid** CTL epitope delivery system consisting of AntpHD peptide vector formulated in liposomes as an alternative approach to bypass the need for SDS. It is proposed that liposomes will prevent degradation of the Ag in vivo and will deliver AntpHD recombinant peptide to the cytosol of APCs. We show in this work that dendritic cells incubated with AntpHD-fused peptide in liposomes can present MHC class I-restricted peptide and induce CTL response with a minimal amount of Ag. Intracellular processing studies have shown that encapsulated AntpHD recombinant peptide is endocytized before entering the cytosol, where it is processed by the proteasome complex. The processed liposomal peptides are then transported to the endoplasmic reticulum. The increase of the CTL response induced by AntpHD-fused peptide in liposomes correlates with this active transport to the class I-processing pathway. In vivo studies demonstrated that positively charged liposomes increase the immunogenicity of AntpHD-Cw3 when injected s.c. in mice in comparison to SDS. Moreover, addition of **CpG** oligodeoxynucleotide **immunostimulatory** sequences further increase the CD8+ T cell response. This strategy combining lipid-based carriers with AntpHD peptide to target poorly immunogenic Ags into the MHC class I processing pathway represents a novel approach for CTL vaccines that may have important applications for development of cancer vaccines.

L19 ANSWER 4 OF 19 MEDLINE on STN
 AN 2001475987 MEDLINE
 DN 21410876 PubMed ID: 11519128
 TI DNA vaccine.
 AU Sato Y
 CS Department of Internal Medicine II, Fukushima Medical University, School of Medicine, Fukushima 960-1295.
 SO RINSHO BYORI. JAPANESE JOURNAL OF CLINICAL PATHOLOGY, (2001 Jul) 49 (7)

precursors and dendritic cells. Protein vaccination in combination with repeated **CpG** therapy was effective in delaying tumor cell growth and extending survival in mice bearing melanoma tumors. These findings support the contention that repeated administration of **CpG** -oligonucleotides enhances the effect of peptide and protein vaccines leading to potent anti-tumor responses, presumably through the induction of Th1 and dendritic cells, which are essential for optimal CTL responses. The **immunostimulatory** properties of **CpG** motifs may be key in inducing a consistent long term immunity to tumor-associated Ags when using peptides or proteins as T cell-inducing vaccines.

- L19 ANSWER 6 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 2003230843 EMBASE
 TI Technological advances to increase immunogenicity of DNA vaccines.
 AU Lemieux P.
 CS Dr. P. Lemieux, Gene Therapy Department, Supratek Pharma Inc., Building 18, 531 Boul. Des Praires, Laval, Que. H7B 1B7, Canada. plemieux007@hotmail.com
 SO Expert Review of Vaccines, (2002) 1/1 (85-93).
 Refs: 65
 ISSN: 1476-0584 CODEN: ERVXAX
 CY United Kingdom
 DT Journal; General Review
 FS 004 Microbiology
 016 Cancer
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 039 Pharmacy
 LA English
 SL English
 AB The latest clinical data obtained with DNA vaccines against HIV and **malaria** have shown promise, but it is clear that when DNA vaccines are compared with other vaccine vector delivery systems, there is still room for improvement. Further development is more than possible, based on the wealth of information accumulating on methods and approaches to increase immunogenicity of DNA vaccines. Thus, the goal of this review is to summarize some of the latest technological advances to increase immunogenicity of DNA vaccines administered by the im. and id. routes. By means of examples, the review will be intended to focus only on recent developments reported in the last 2 years and likely to go towards the improvement of mucosal, humoral and cellular immune responses mostly against cancer and infectious disease antigens.
- L19 ANSWER 7 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 2003220506 EMBASE
 TI Recent advances in veterinary vaccine adjuvants.
 AU Singh M.; O'Hagan D.T.
 CS M. Singh, Chiron Vaccines Research, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, United States. manmohan_singh@chiron.com
 SO International Journal for Parasitology, (2003) 33/5-6 (469-478).
 Refs: 110
 ISSN: 0020-7519 CODEN: IJPYBT
 CY United Kingdom
 DT Journal; General Review
 FS 004 Microbiology
 026 Immunology, Serology and Transplantation
 027 Biophysics, Bioengineering and Medical Instrumentation
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LA English
 SL English
 AB Next generation veterinary vaccines are going to mainly comprise of either subunit or inactivated bacteria/viruses. These vaccines would require

optimal adjuvants and delivery systems to accord long-term protection from infectious diseases in animals. There is an urgent need for the development of new and improved veterinary and human vaccine adjuvants. Adjuvants can be broadly divided into two classes, based on their principal mechanisms of action: vaccine delivery systems and 'immunostimulatory' adjuvants'. Vaccine delivery systems are generally particulate e.g. emulsions, microparticles, ISCOMS and liposomes, and mainly function to target associated antigens into antigen presenting cells (APC). In contrast, immunostimulatory adjuvants are predominantly derived from pathogens and often represent pathogen associated molecular patterns, e.g. LPS, MPL and CpG DNA, which activate cells of the innate immune system. Recent progress in innate immunity is beginning to yield insight into the initiation of immune responses and the ways in which immunostimulatory adjuvants might enhance this process in animals and humans alike. .COPYRGT. 2003 Australian Society for Parasitology Inc. Published by Elsevier Science Ltd. All rights reserved.

- L19 ANSWER 8 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 2003194353 EMBASE
 TI Vaccine adjuvants.
 AU Glenn G.
 CS Dr. G. Glenn, IOMAI Corporation, 20 Firstfield Road, Gaithersburg, MD 20878, United States. gglenn@iomai.com
 SO Expert Review of Vaccines, (2003) 2/2 (163-164).
 Refs: 7
 ISSN: 1476-0584 CODEN: ERVXAX
 CY United Kingdom
 DT Journal; Editorial
 FS 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 039 Pharmacy
 LA English
- L19 ANSWER 9 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 2003161017 EMBASE
 TI Cytokine, chemokine, and costimulatory molecule modulation to enhance efficacy of HIV vaccines.
 AU Ahlers J.D.; Belyakov I.M.; Berzofsky J.A.
 CS J.A. Berzofsky, Molec. Immunogen./Vaccine Res. Sec., Metabolism Branch, National Cancer Institute, Building 10, Bethesda, MD 20892-1578, United States. jahlers@niaid.nih.gov
 SO Current Molecular Medicine, (2003) 3/3 (285-301).
 Refs: 206
 ISSN: 1566-5240 CODEN: CMMUBP
 CY Netherlands
 DT Journal; General Review
 FS 004 Microbiology
 026 Immunology, Serology and Transplantation
 030 Pharmacology
 037 Drug Literature Index
 039 Pharmacy
 LA English
 SL English
 AB Understanding key intervention points in developing immune responses may allow the rational inclusion of biological adjuvants into vaccines that could potentiate the immune response both quantitatively and qualitatively and enhance effective memory responses. Cytokine and chemokine combinations can potentially help target antigen to the appropriate antigen presenting cell and initiate maturation of these presenting cells, attract cells expressing different chemokine receptors, steer cellular immune responses toward Th1 and CD8 CTL, and enhance systemic and mucosal IgG and secretory IgA antibodies and determine their isotype balance.

DNA region, where at least one terminus of the oligonucleotide comprises RNA, and at least one target antigen;

(3) a method of stimulating innate immunity comprising administering at least one oligonucleotide comprising both an RNA region and a DNA region, where at least one terminus of the oligonucleotide comprises RNA, and where the oligonucleotide is associated with a physiological carrier or delivery system;

(4) a method of stimulating global immunity comprising administering at least one oligonucleotide comprising both an RNA region and a DNA region, where at least one terminus of the oligonucleotide comprises RNA, and where the oligonucleotide is associated with a physiological carrier or delivery system;

(5) methods of stimulating a cellular immune response or a humoral immune response comprising administering the vaccine of (1b); and

(6) a method of making a vaccine comprising associating:

(a) at least one oligonucleotide comprising both an RNA region and a DNA region, where at least one terminus of the oligonucleotide comprises RNA; and

(b) a physiological carrier or delivery system.

ACTIVITY - Immunostimulant; antiallergic; cytostatic; antimicrobial; immunosuppressive; anti-HIV; protozoacide; virucide; hepatotropic; antiinflammatory; antibacterial.

MECHANISM OF ACTION - Gene therapy; cytokine stimulator; vaccine. The stimulation of cytokines interleukin-6 (IL-6) and interferon gamma (IFN-gamma) in human peripheral lymphocytes cultured from four healthy volunteer subjects, designated S1 through S4, was assayed using standard methods. Oligonucleotides DDD and RDR were added to the media of cultured cells to final concentrations of 0.3, 3, or 30 micro g/ml. 24 hours after oligonucleotide addition, Th1 and Th2-type cytokine levels in the media were determined by enzyme linked immunoabsorbant assay (ELISA). The **hybrid** DNA/RNA oligonucleotides stimulated the production of cytokines implicated in eliciting both Th1 (IFN-gamma) and Th2 T (IL-6) type responses in human peripheral lymphocytes. At the highest concentrations tested, for example, the **hybrid** RDR molecule was 3-fold more effective at inducing IFN-gamma and 5-fold more effective at stimulating the release of IL-6.

USE - The composition is useful for enhancing an immune response or inducing cytokines. The compositions comprising the oligonucleotides are useful as vaccine adjuvants and in treating diseases, e.g. pathogenic infection, (non-)malignant tumors (e.g. cancers of the brain, lung, ovary, breast, prostate or colon, or carcinomas and sarcomas), autoimmune disease or allergy (e.g. allergic rhinitis, hay fever or food allergies), lyme disease, hepatitis, HIV or **malaria**. The composition is also useful for treating, preventing or ameliorating the symptoms resulting from exposure to a bio-warfare agent, e.g. Ebola, Anthrax or Listeria.

Dwg.0/0

L19 ANSWER 13 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2001-112392 [12] WPIDS

DNC C2001-033426

TI New vaccine formulation, useful for preventing and treating **plasmodium** infection in a patient, comprises **malaria** antigen and **immunostimulatory CpG** oligonucleotide.

DC B04 D16

IN COHEN, J; GARCON, N; VOSS, G

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS

CYC 95

PI WO 2001000231 A2 20010104 (200112)* EN 21p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000059777 A 20010131 (200124)

EP 1198243 A2 20020424 (200235) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

ADT WO 2001000231 A2 WO 2000-EP5841 20000623; AU 2000059777 A AU 2000-59777
20000623; EP 1198243 A2 EP 2000-945810 20000623, WO 2000-EP5841 20000623

FDT AU 2000059777 A Based on WO 200100231; EP 1198243 A2 Based on WO 200100231

PRAI GB 1999-15204 19990629

AB WO 200100231 A UPAB: 20010302

NOVELTY - A vaccine formulation (I) comprising a **malaria** antigen
(II) and an **immunostimulatory CpG** oligonucleotide
(III), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the
production of (I), which comprises admixing (II) and (III).

ACTIVITY - Antimalarial; protozoacide.

MECHANISM OF ACTION - Vaccine (claimed).

5 rhesus monkeys per group were immunized twice intramuscularly with
500 micro l of vaccine at a four week-interval. Sera and peripheral blood
mononuclear cells were taken at several occasions. HBsAg-specific
(undefined) antibodies in monkey sera were determined in an ELISA (enzyme
linked immunosorbant assay). Lymphoproliferation was assessed by using
density gradient-purified PBMC (peripheral blood mononuclear cells) from
immunized rhesus monkeys. Cells were seeded in quadruplicates at 1
multiply 105 in 100 micro l RPMI (undefined)/5% FCS (fetal calf serum) per
well in round bottom 96 well plates. Then another 100 micro l of medium
alone or containing soluble **RTS,R** (10 micro g/ml **hybrid**
protein with **CpG** oligonucleotide) were added and parallel
cultures were incubated for 48 hours. Thereafter, 100 micro l culture
supernatant were replaced by fresh medium containing 1 micro Ci
(3H)-thymidine. After 16 hours cells were harvested onto filter plates and
incorporated radioactivity was determined in a beta -counter. Results
showed that analysis of HBsAg-specific antibodies in sera of the monkeys
revealed that all animals in the two groups had developed specific immune
responses.

USE - (I) is useful as a medicament for preventing or treating
plasmodium infection in a patient (claimed).

Dwg.0/4

L19 ANSWER 14 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2000-687101 [67] WPIDS

CR 2002-471376 [50]

DNC C2000-209017

TI **Adjuvant** composition comprising saponin and
immunostimulatory oligonucleotide **CpG**, useful for
producing vaccine formulations for prophylaxis and treatment of cancers,
allergy and Alzheimer's disease.

DC B04 D16

IN FRIEDE, M; GARCON, N; HERMAND, P; GERARD, C M G

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS

CYC 92

PI WO 2000062800 A2 20001026 (200067)* EN 52p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE
ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000041149 A 20001102 (200107)

NO 2001005073 A 20011122 (200211)

BR 2000010612 A 20020213 (200220)

CZ 2001003774 A3 20020313 (200223)

EP 1187629 A2 20020320 (200227) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

HU 2002000815 A2 20020828 (200264)
JP 2002542203 W 20021210 (200301) 65p
ZA 2001008619 A 20021127 (200305) 70p
CN 1372473 A 20021002 (200307)
KR 2002067617 A 20020823 (200310)
US 6544518 B1 20030408 (200327)

ADT WO 2000062800 A2 WO 2000-EP2920 20000404; AU 2000041149 A AU 2000-41149
20000404; NO 2001005073 A WO 2000-EP2920 20000404, NO 2001-5073 20011018;
BR 2000010612 A BR 2000-10612 20000404, WO 2000-EP2920 20000404; CZ
2001003774 A3 WO 2000-EP2920 20000404, CZ 2001-3774 20000404; EP 1187629
A2 EP 2000-920647 20000404, WO 2000-EP2920 20000404; HU 2002000815 A2 WO
2000-EP2920 20000404, HU 2002-815 20000404; JP 2002542203 W JP 2000-611936
20000404, WO 2000-EP2920 20000404; ZA 2001008619 A ZA 2001-8619 20011019;
CN 1372473 A CN 2000-808836 20000404; KR 2002067617 A KR 2001-713357
20011019; US 6544518 B1 CIP of US 1999-301829 19990429, CIP of WO
2000-EP2920 20000404, US 2000-690921 20001018

FDT AU 2000041149 A Based on WO 200062800; BR 2000010612 A Based on WO
200062800; CZ 2001003774 A3 Based on WO 200062800; EP 1187629 A2 Based on
WO 200062800; HU 2002000815 A2 Based on WO 200062800; JP 2002542203 W
Based on WO 200062800

PRAI US 1999-301829 19990429; GB 1999-8885 19990419

AB WO 200062800 A UPAB: 20030429

NOVELTY - An **adjuvant** composition (I) comprising a saponin and
an **immunostimulatory** oligonucleotide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
following:

(1) a vaccine composition (II) comprising (I) and an antigen;
(2) a delivery device pre-filled with (II) designed to administer the
vaccine systemically;

(3) use of a vaccine as a medicament;
(4) use of a combination of saponin and **CpG** molecule (
immunostimulatory oligonucleotides containing unmethylated
CpG dinucleotides) in the manufacture of a vaccine for the
prophylaxis and treatment of viral, bacterial and parasitic infections,
allergy, cancer or other chronic disorders;

(5) making (I) involves admixing a saponin with an
immunostimulatory oligonucleotide and optionally a carrier; and
(6) making (II) involves admixing saponin, **immunostimulatory**
oligonucleotide, an antigen and optionally a carrier.

ACTIVITY - Cytostatic; antiallergic; antiatherosclerotic; nootropic;
neuroprotective; antibacterial; antiviral; antiparasitic.

MECHANISM OF ACTION - Vaccine. The biological activity of (II) was
tested in mice. Female Balb/c mice (5 animals per group), aged 8 weeks,
were immunized intramuscularly with lipo-OspA (1 mu g) formulated onto
alum (50 mu g). After 3 months, the mice were boosted intranasally with a
solution containing 5 mu g lipo-OspA in either A, B, C, D or E.

(A) PBS;

(B) 20 mu g **CpG** 1001 (TCC ATG AGC TTC CTG ACG TT, Kreig
1826);

(C) 5 micro g QS21;

(D) 20 micro g **CpG** 1001 + 5 micro g QS21; or

(E) by intramuscular injection of 1 micro g lipo-OspA absorbed onto
alum (50 micro g).

OspA-specific serum IgG in mice was measured by enzyme linked
immunoabsorbant assay (ELISA). **CpG** as well as QS21 significantly
improved the intranasal boosting of systemic antibodies to Lipo-OspA.
Moreover, when both adjuvants were combined, a synergistic effect of those
responses was clearly demonstrated, especially in terms of LA2 antibodies.
Humoral responses elicited in the presence of QS21 and **CpG** were
significantly higher than those induced by the parenteral booster.

USE - A vaccine composition containing (I) administered systemically,

is useful for inducing an immune response in an individual and for preventing or treating an individual susceptible to or suffering from a disease. Diseases include prostate, breast, colorectal, lung, pancreatic, renal, ovarian or melanoma cancers; non-cancer chronic disorders such as allergy, Alzheimer and atherosclerosis. The vaccine is useful for prophylaxis and treatment of viral, bacterial and parasitic infections too (claimed).

Dwg.0/12

L19 ANSWER 15 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 1999-494293 [41] WPIDS
 DNC C1999-144897
 TI New protein derivatives used in cancer vaccine therapy for treating a range of cancers including melanomas, carcinomas and cancers of breast.
 DC B04 D16
 IN BASSOLS, C V; COHEN, J; SILVA, T C; SLAQUI, M M; CABEZON, S T; SLAQUI, M; VINALS, B C; CABEZON SILVA, T; VINALS BASSOLS, C; SLAQUI, M M
 PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
 CYC 86
 PI WO 9940188 A2 19990812 (199941)* EN 74p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
 GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 UA UG US UZ VN YU ZW
 AU 9927220 A 19990823 (200005)
 ZA 9900872 A 20000927 (200050) 75p
 NO 2000003958 A 20001004 (200058)
 EP 1053325 A2 20001122 (200061) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
 BR 9907691 A 20001114 (200064)
 CZ 2000002869 A3 20010117 (200107)
 CN 1295616 A 20010516 (200146)
 AU 737337 B 20010816 (200153)
 KR 2001040675 A 20010515 (200167)
 MX 2000007677 A1 20010201 (200168)
 HU 2001002639 A2 20011128 (200209)
 JP 2002502604 W 20020129 (200211) 91p
 NZ 506086 A 20030131 (200319)
 ADT WO 9940188 A2 WO 1999-EP660 19990202; AU 9927220 A AU 1999-27220 19990202;
 ZA 9900872 A ZA 1999-872 19990204; NO 2000003958 A WO 1999-EP660 19990202,
 NO 2000-3958 20000804; EP 1053325 A2 EP 1999-907476 19990202, WO
 1999-EP660 19990202; BR 9907691 A BR 1999-7691 19990202, WO 1999-EP660
 19990202; CZ 2000002869 A3 WO 1999-EP660 19990202, CZ 2000-2869 19990202;
 CN 1295616 A CN 1999-804604 19990202; AU 737337 B AU 1999-27220 19990202;
 KR 2001040675 A KR 2000-708550 20000804; MX 2000007677 A1 MX 2000-7677
 20000804; HU 2001002639 A2 WO 1999-EP660 19990202, HU 2001-2639 19990202;
 JP 2002502604 W WO 1999-EP660 19990202, JP 2000-530602 19990202; NZ 506086
 A NZ 1999-506086 19990202, WO 1999-EP660 19990202
 FDT AU 9927220 A Based on WO 9940188; EP 1053325 A2 Based on WO 9940188; BR
 9907691 A Based on WO 9940188; CZ 2000002869 A3 Based on WO 9940188; AU
 737337 B Previous Publ. AU 9927220, Based on WO 9940188; HU 2001002639 A2
 Based on WO 9940188; JP 2002502604 W Based on WO 9940188; NZ 506086 A
 Based on WO 9940188
 PRAI GB 1998-2650 19980206; GB 1998-2543 19980205
 AB WO 9940188 A UPAB: 19991011
 NOVELTY - Tumour-associated antigen derivatives (A) obtained from MAGE
 (melanoma antigen) family are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) nucleic acid sequence encoding (A);
- (2) a vector comprising the nucleic acid of (1);

- (3) a host cell transformed with the vector of (2);
- (4) a vaccine containing (A) or the nucleic acid of (1);
- (5) a purification process of MAGE protein or its derivatives comprises:
 - (a) reducing disulfide bonds;
 - (b) blocking resulting free thiol group with a blocking group; and
 - (c) subjecting the resulting derivative to one or more chromatographic purification steps;
- (6) a process for vaccine production comprises:
 - (a) purification of MAGE protein or its derivative by the process of (5); and
 - (b) formulating the resulting protein as a vaccine.

ACTIVITY - Cytostatic

MECHANISM OF ACTION - Vaccine.

The vaccine Lipo D 1/3 Mage 3 His/SBAS2 was tested for its antibody response using 3 groups of five Rhesus monkeys (RH). The first two groups, group 1 and 2 received **RTS**, S and gpl20 (all undefined) with adjuvants SBAS2 or SB26T and were used as positive control. The vaccine Lipo D 1/3 Mage 3 His/SBA2 was administered to the right leg of group 3 RH at day 0, 28 and 84 by intramuscular injection at posterior part of leg. Small unheparinized blood samples of 3 ml were collected from femoral vein every 14 days and was allowed to clot for 1 hour. It was then centrifuged at 2500 rpm for 10 min. and serum was removed. The resulting contents were frozen at 20 deg. C and kinetics of antibody response was determined by ELISA. Result showed a clear boost in Mage 3 specific total antibody titre (no specific values given) in 3 out of 5 animals after second and third injection.

USE - The vaccine is used in medicine for immunotherapeutically treating patients suffering from melanomas or other MAGE associated tumors like breast, bladder, lung and non-small cell lung cancer, head and squamous cell carcinoma, colon carcinoma and esophagus carcinoma.

ADVANTAGE - The expression enhancer partners associated with the antigen increases the levels of protein expression. The derivatives like affinity tags helps in easier purification. Blocking agents used in the purification step prevents aggregation of product and therefore ensures stability for downward purification.

Dwg.0/19

L19 ANSWER 16 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 1999-405369 [34] WPIDS
 CR 1999-405485 [34]
 DNC C1999-119689
 TI A vaccine composition for inducing a immune response to T-independent type 1 or type 2 antigen or polysaccharide conjugate antigen.
 DC B04 D16
 IN DALEMANS, W L J; LAFERRIERE, C A J; PRIEELS, J; GERARD, C M; DALEMANS, W; GERARD, C M G
 PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
 CYC 86
 PI WO 9933488 A2 19990708 (199934)* EN 35p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
 GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 UA UG US UZ VN YU ZW
 AU 9924190 A 19990719 (199951)
 ZA 9811849 A 20000726 (200042) 35p
 EP 1039930 A2 20001004 (200050) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
 NO 2000003303 A 20000804 (200050)
 NO 2000003302 A 20000818 (200052)
 BR 9814483 A 20001010 (200055)

CZ 2000002375 A3 20001115 (200064)
 CN 1284884 A 20010221 (200131)
 CN 1284885 A 20010221 (200131)
 AU 736099 B 20010726 (200149)
 KR 2001033613 A 20010425 (200164)
 KR 2001033618 A 20010425 (200164)
 MX 2000006323 A1 20010201 (200168)
 MX 2000006324 A1 20010201 (200168)
 JP 2001527050 W 20011225 (200204) 42p
 HU 2001003085 A2 20011128 (200209)
 NZ 505107 A 20030328 (200325)

ADT WO 9933488 A2 WO 1998-EP8562 19981218; AU 9924190 A AU 1999-24190 19981218; ZA 9811849 A ZA 1998-11849 19981223; EP 1039930 A2 EP 1998-966705 19981218, WO 1998-EP8562 19981218; NO 2000003303 A WO 1998-EP8563 19981218, NO 2000-3303 20000623; NO 2000003302 A WO 1998-EP8562 19981218, NO 2000-3302 20000623; BR 9814483 A BR 1998-14483 19981218, WO 1998-EP8562 19981218; CZ 2000002375 A3 WO 1998-EP8562 19981218, CZ 2000-2375 19981218; CN 1284884 A CN 1998-813794 19981218; CN 1284885 A CN 1998-813795 19981218; AU 736099 B AU 1999-24190 19981218; KR 2001033613 A KR 2000-707126 20000624; KR 2001033618 A KR 2000-707131 20000624; MX 2000006323 A1 MX 2000-6323 20000623; MX 2000006324 A1 MX 2000-6324 20000623; JP 2001527050 W WO 1998-EP8562 19981218, JP 2000-526239 19981218; HU 2001003085 A2 WO 1998-EP8562 19981218, HU 2001-3085 19981218; NZ 505107 A NZ 1998-505107 19981218, WO 1998-EP8562 19981218

FDT AU 9924190 A Based on WO 9933488; EP 1039930 A2 Based on WO 9933488; BR 9814483 A Based on WO 9933488; CZ 2000002375 A3 Based on WO 9933488; AU 736099 B Previous Publ. AU 9924190, Based on WO 9933488; JP 2001527050 W Based on WO 9933488; HU 2001003085 A2 Based on WO 9933488; NZ 505107 A Based on WO 9933488

PRAI GB 1997-27262 19971224

AB WO 9933488 A UPAB: 20030416

NOVELTY - A formulation (A) comprising a **CpG** oligonucleotide and T-independent type 1 or type 2 antigens or polysaccharide conjugate antigen, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a formulation as in (A), wherein the **CpG** oligonucleotide is selected from the sequences of formula (I)-(IV):
 GCTACTGGTACG TACATTC AGACGGC TCTT (I); ACTATCTAAACGCTAATGGTGCTATGGCGACAG GATGGCT (II); TCC ATG ACG TTC CTG ACG TT (III); and TCT CCC AGC GTG CGC CAT (IV);

(2) a vaccine composition comprising the formulation, for use in medicine; and

(3) a method of inducing an immune response to T independent type 1 or type 2 antigen or a polysaccharide conjugate antigen, comprising administering a safe and effective amount of the formulation to a patient.

USE - The vaccine composition comprising the formulation is used for inducing a immune response to T-independent type 1 or type 2 antigen or polysaccharide conjugate antigen

ADVANTAGE - The use of **immunostimulatory CpG** oligonucleotide acts as an **adjuvant** to pneumococcal polysaccharides.

Dwg.0/2

L19 ANSWER 17 OF 19 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

AN 2002-19865 BIOTECHDS

TI CYP1B1 polynucleotide for inducing immune response against cancer, has transcriptional units encoding polypeptides, and lack sequences found in untranslated region of naturally occurring forms of transcript;
 vector-mediated cytochrome-P450 gene transfer and expression in host cell for nucleic acid vaccine and gene therapy

AU AZIZ N; HEDLEY M L; URBAN R G; TOMLINSON A J; COLE G

PA ZYCOS INC
PI WO 2002042325 30 May 2002
AI WO 2000-US45170 31 Oct 2000
PRAI US 2001-298428 15 Jun 2001
DT Patent
LA English
OS WPI: 2002-557504 [59]
AB DERWENT ABSTRACT:

NOVELTY - A polynucleotide (I) comprising a transcriptional unit (TU), having sequence encoding CYP1B1, or protein comprising a peptide that binds to a major histocompatibility complex class I or II molecule, where TU does not contain translational repressor element operably linked to coding sequence or 150 consecutive nucleotides of sequence of 1-362 or 2011-5128 of 5110 base pairs sequence as given in specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) polynucleotide (II) comprising a TU encoding a **hybrid** polypeptide which comprises a first and a second segment of CYP1B1, which are either contiguous or separated by a spacer amino acid or spacer peptide, where the two segments are each at least eight amino acids in length, and are non-contiguous portions of CYP1B1; (2) a composition (C1) comprising (I), and an **immunostimulatory** agent or nucleic acid encoding the agent; (3) a therapeutic composition (C2) comprising (I) and a carrier; and (4) a microparticle (MP) comprising a polymeric matrix or shell and (I).

BIOTECHNOLOGY - Preferred Polynucleotide: In (I), the polypeptide comprises a segment of CYP1B1 that is eight amino acids and preferably comprises a sequence (S1) Phe Leu Asp Pro Arg Pro Leu Thr Val, which is less than 100 amino acids in length and further comprises a targeting signal, where TU comprises an RNA stabilization sequence. (I) further comprises an inducible promoter sequence operably linked to TU, where TU does not contain any of sequence selected from 3-9, or 15-17, more preferably TU does not contain 50 more preferably 10 consecutive nucleotides of sequence 18 or 19, and TU comprises an inducible promoter sequence, and a translational regulatory sequence operably linked to the coding sequence, where the regulatory sequence is an iron responsive sequence. In (II), the **hybrid** polypeptide further comprises a third segment of CYP1B1, which is of at least eight amino acids, where the first and third and second and third segments are non-contiguous portion of CYP1B1, and first segment comprises the sequence (S1).

Preferred Composition: In C1, the **immunostimulatory** agent is a **CpG** containing oligonucleotide of 18-30 nucleotides, and is preferably interleukin (IL)-12, interferon (IFN)-gamma or a bacterial polypeptide, or is a lipid, nucleic acid, or carbohydrate.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - T or B cell response inducer (claimed). Three strains of mice (C3H, C57/B16 and Balb/c) were injected (intramuscularly) with 100 microg of pcDNA3-hulB1, which encodes a protein that is processed, presented and can stimulate major histocompatibility complex (MHC) class II CD4+ T cell response. Mice were boosted on day 14 with the same dose of pcDNA3-hulB1. Spleens were harvested on day 27 and IFN-g ELISPOT assays were performed using CD4+T cell enriched splenocytes tested against syngeneic antigen presenting cell (APC) pulsed with peptide. In addition, CD4+T cells isolated from naive mice were screened to serve as a negative control. All CD4+T cells were screened against a panel of synthetic CYP1B1 30 mer peptides, phytohemagglutinin (PHA), and hepatitis B virus (HBV)-2. The results of the above assay showed that CYP1B1 peptides stimulated a response in each of the three mouse strains tested. All reported values represent IFN-g Spot Forming Cells (SFC)/1,000,000 CD4+T cells.

USE - (I) or MP is useful for inducing an immune response especially T or B cell response, in a mammal suffering from or is at risk for cancer, where the method preferably comprises detecting expression of CYP1B1 in a tumor of a mammal, and administering (I), where the mammal

belongs to a species especially human, and CYP1B1 or its portion is identical to a sequence of a naturally occurring CYP1B1 polypeptide of a different species which is a rodent preferably a rat or mouse. (I) is further useful for reducing tumor growth or tumor activity in a mammal by identifying a mammal having a tumor, administering (I), and detecting a reduction in the size or activity of the tumor (claimed).

ADMINISTRATION - (I) is administered subcutaneously or intramuscularly (claimed), or intravenously, intraarterially, intradermally, intraperitoneally, intranasally, intravaginally or intrarectally. Dosage of (I) is 10-1000 microg.

EXAMPLE - cDNAs encoding human CYP1B1 and CYP1B1-delta3 were each cloned into two different plasmid expression vectors, pCDNA-3 and p3K. The CYP1B1 nucleic acid constructs contained a cDNA coding for 543 amino acid protein, but lacking all untranslated regions of CYP1B1. The CYP1B1-delta3 construct contained three substitutions, relative to the wild type CYP1B1, at amino acid 61: Gly changed to a Glu; amino acid 365: Gly changed to a Trp. The expression vectors pCDNA3-CYPHulB1, p3K-CYPHulB1, pCDNA3-control vectors pCDNA3 and p3K were purified from transformed Escherichia coli. Each construct was sequenced to confirm the introduction of the desired changes. Additional CYP1B1 constructs were made as follows. Deletions were introduced using polymerase chain reaction (PCR), in the background of pCDNA3hulBld5, which encodes a human CYP1B1 protein in which five amino acids are substituted: W57C, G61E, G365W, P379L, and E387K. Upstream primers contained a restriction site and an ATG codon in frame with the subsequent coding sequences. Downstream primers contained the appropriate CYP1B1 coding sequences, followed by the stop codon, and a restriction site for cloning purposes. pCDNA3hulB1-deltaPPGP encoded the whole CYP1B1 protein, with the exception of amino acids 51 to 54 (PPGP), which were deleted. The pCDNAhulB1-F1R1 encoded protein contained a deletion of the first 60 amino acids of CYP1B1, and the pCDNA3hulB1-F1R2 protein contained the same N-terminal deletion, in addition to the last 82 amino acids of the CYP1B1 protein. The pCDNA3hulB1-F2R2 encoded protein contained the same N-terminal deletion, in addition to the last 82 amino acids of CYP1B1. The pCDNA3hulB1-F3R1 protein contained a deletion of the first 292 amino acids of CYP1B1, and pCDNA3hulB1-F3R2 contained the same N-terminal deletion, in addition to the last 82 amino acids of the CYP1B1 protein. (73 pages)

L19 ANSWER 18 OF 19 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AN 2002-11156 BIOTECHDS
TI Fusion protein useful in vaccine compositions for treating allergies and asthma, comprises a Pathogen Associated Molecular Pattern and an antigen; recombinant fusion protein production for use in recombinant vaccine against cancer, asthma, allergy, herpes, infection, tuberculosis, etc.
AU MEDZHITOV R M P D
PA UNIV YALE
PI WO 2002009748 7 Feb 2002
AI WO 2000-US24228 31 Jul 2000
PRAI US 2001-282604 9 Apr 2001
DT Patent
LA English
OS WPI: 2002-217100 [27]
AB DERWENT ABSTRACT:
NOVELTY - A fusion protein (I) comprising an isolated Pathogen Associated Molecular Pattern (PAMP), its **immunostimulatory** portion or derivative, and an antigen (II), its immunogenic portion or derivative, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a recombinant vector (III) comprising nucleotides encoding (I); (2) a host cell (IV) comprising (III); (3) producing (I); (4) a vaccine (V) comprising (I); (5) treating (M1) a subject, by: (a) administering (V) and antibodies (Abs) or activated immune cells directed

against (II), to a subject; or (b) administering (V) and a chemotherapeutic or anti-angiogenic agent; (6) stimulating (M2) an innate immune response in an animal and thus enhancing the adaptive immune response to a foreign or self-antigen; and (7) a vaccine comprising a PAMP conjugated with a foreign or self-antigen that stimulates an innate immune response in an animal and thus enhances the adaptive immune response to a foreign or self-antigen but does not lead to undesirable levels of inflammation.

WIDER DISCLOSURE - The following are disclosed: (1) nucleic acid molecules encoding (I); (2) peptide mimetics of non-protein PAMPs; (3) derivatives, portions or peptides of PAMPs that are recognized by the innate immune system; (4) a chimeric construct comprising **CpG** or **CpG-DNA**, and an antigen; (5) a mimetic of a three-dimensional structure of PAMP protein or its antigen; (6) conservative variants of naturally occurring protein PAMPs, peptides or peptide mimetics of PAMPs that recognize the corresponding PAMP receptor proteins; and (7) a combination of more than one other therapeutics with (V).

BIOTECHNOLOGY - Preparation: (I) is obtained by culturing (IV) and isolating (I) produced by the cell (claimed). Preferred Proteins: PAMP is a peptide, protein, lipoprotein or glycoprotein, e.g. a ligand for a pattern recognition receptor (PRR). (II) is obtainable from bacteria, viruses, fungi, yeast, protozoa, metazoa, tumors, malignant cells, abnormal neural cells, arthritic lesions, cardiovascular lesions, plants, animals, humans, allergens or hormones, and is microbe-related, allergen-related or related to abnormal human or animal cells. PAMP and (II) are linked by a chemical linker. The PAMP and (II) are separated by a spacer. PAMP is bacterial lipoprotein (BLP) comprising a sequence of 78 amino acids fully defined in the specification. (II) is selected from any one of the antigens given in the specification. PAMP is a peptide mimetic of a non-protein PAMP and/or (II) is a peptide mimetic of a non-protein antigen. (I) comprises a leader sequence, glycosylation or lipidation consensus sequence and an antigen sequence. The leader sequence signals post-translational glycosylation or lipidation of the consensus sequence. The leader peptide comprises one of sequences of (A) - (E). The consensus sequence is CXXN. (II) is associated with disease, allergen-related or related to abnormal human or animal cells. PAMP is selected from *Borrelia ospA*, *ospB* or *ospC*, the lipidated tetrapeptide of bacterial lipoprotein and *Klebsiella ompA*. Preferred Cell: (IV) is a bacterial, yeast, plant, animal or insect cell. (IV) is a bacteria, that produces the PAMP naturally, or that lipidates the PAMP. Preferred Method: In M1, Abs are monoclonal. The chemotherapeutic agent is an anti-cancer agent. In M2, the innate immune response is stimulated by activating one or more Toll-like Receptors. The adaptive immune response is enhanced by the activation of antigen presenting cells (APCs) by the activation of one or more Toll-like Receptors. Met Lys Ala Thr Lys Leu Val Leu Gly Ala Val Ile Leu Gly Ser Thr Leu Leu Ala Gly (A) Met Asn Arg Thr Lys Leu Val Leu Gly Ala Val Ile Leu Gly Ser Thr Leu Leu Ala Gly (B) Met Asn Arg Thr Lys Leu Val Leu Gly Ala Val Ile Leu Gly Ser His Ser Ala Gly (C) Met Lys Ala Lys Ile Val Leu Gly Ala Val Ile Leu Ala Ser Gly Leu Leu Ala Gly (D) Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala (E)

ACTIVITY - Antiallergic; antiasthmatic; neuroprotective; nootropic; cytostatic; antimicrobial; immunosuppressive; cardiact; antileprotic; antimalarial; tuberculostatic; dermatological; virucide; protozoacide; antiinflammatory; antiarteriosclerotic.

MECHANISM OF ACTION - Vaccine (claimed); TLR-mediated signaling pathway stimulator; immune response stimulator. To test whether bacterial lipoprotein (BLP)/Ealpha could induce dendritic cells (DC) function, the ability of bone marrow-derived DC to produce interleukin (IL)-6 after stimulation in vitro was determined. Bone marrow dendritic cells were isolated and grown for 5 days in culture in the presence of 1 % granulocyte macrophage-colony stimulating factor (GM-CSF). After 5 days, cells were replated at 250000 cells/well in a 96-well dish and treated

with either Ealpha peptide (0.3 micrograms/ml), lipopolysaccharide (LPS) (100 ng/ml)+Ealpha peptide (0.3 micrograms/ml) or BLP/Ealpha. BLP/Ealpha was able to stimulate IL-6 production in the cells as measured by a sandwich enzyme linked immunosorbant assay (ELISA).

USE - A vaccine (V) comprising (I) is useful for immunizing an animal, preferably mammal e.g. in a human diagnosed with Alzheimer's disease, in combination with surgery or radiation therapy (claimed). (V) is useful for treating a patient susceptible to an allergic response to an allergen, and treating a patient susceptible to or suffering from Alzheimer's disease. (V) is also useful for treating and preventing allergies and asthma, cancer, infectious diseases, autoimmune diseases, neurological diseases, cardiovascular diseases, immune deficiency syndrome, topical and systemic infections, leprosy, tuberculosis, shingles, warts, herpes, **malaria**, gingivitis, atherosclerosis and diseases associated with allergic reactions.

ADMINISTRATION - A vaccine (V) comprising (I) is administered through parenteral, intravenous, oral, suppository or mucosal route (claimed). (V) is also administered through intramuscular, sub-cutaneous or intraperitoneal route. No dosage is specified.

ADVANTAGE - The vaccine provides an efficient way of making and using a single molecule to induce a robust T cell immune response that activates other aspects of adaptive immune response. The vaccine provides an efficient way to produce an immune response to one or more antigens without adverse side effects normally associated with conventional vaccines. The vaccine induced an immune response in the mice that is stronger than that produced by Ealpha peptide mixed with Complete Freund's **Adjuvant** (CFA). The gene fusion expression system avoids the degradation of proteins, especially small peptides, by host proteases. The use of a fusion partner as an affinity handle allows rapid isolation and purification of recombinant peptide. By using different fusion partners, the recombinant product may be localized to different compartments, or it might be secreted. The vaccine induces strong immune response against target antigen with minimal undesired inflammatory reaction, as well as minimal instances of autoimmune disease.

EXAMPLE - In order to produce a model vaccine cassette, a Pathogen-Associated Molecular Pattern (PAMP) was fused to the characterized mouse antigen, Ealpha. PAMP, a bacterial lipoprotein (BLP), was known to stimulate innate immune responses through the receptor, Toll-like-receptor-2 (TLR-2). The protein sequence (S1) of BLP used in the vaccine cassette for fusion with an antigen of interest comprised 78 amino acids, given in the specification. The leader sequence included amino acids 1 - 20 of S1. The first cysteine (amino acid number 21 of S1) was lipidated in bacteria (can occur only in bacteria), which was essential for BLP recognition by Toll and TLRs. The C-terminal lysine (amino acid number 78 of S1) was mutated to increase the yield of a recombinant vaccine, as the lysine can form a covalent bond with the peptidoglycan. To assist in identification and purification of the antigen, a hexa-histidine tag was engineered on the C-terminal of the protein. The final construct is given in the specification. The fusion protein was expressed in bacteria, induced with isopropyl-betaD-thiogalactopyranoside (IPTG) and protein was purified by lysis. The lysate was passed over a 100 ml Q-Sepharose ion exchange column, eluted and positive fractions were identified by immunoblotting using an antibody to the Histidine tag. (139 pages)

L19 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:276663 CAPLUS

DN 138:302632

TI **Adjuvant** compns. and uses thereof in vaccines

IN Friede, Martin; Garcon, Nathalie; Gerard, Catherine Marie Ghislaine; Hermand, Philippe

PA Smithkline Beecham Biologicals S.A., Belg.

SO U.S., 29 pp., Cont.-in-part of Appl. No. PCT/EP00/02920.

CODEN: USXXAM

DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6544518	B1	20030408	US 2000-690921	20001018
	US 6558670	B1	20030506	US 1999-301829	19990429
	WO 2000062800	A2	20001026	WO 2000-EP2920	20000404
	WO 2000062800	A3	20010111		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	WO 2002032450	A2	20020425	WO 2001-EP11984	20011016
	WO 2002032450	A3	20021010		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2002044337	A5	20020429	AU 2002-44337	20011016
	EP 1326638	A2	20030716	EP 2001-987671	20011016
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	GB 1999-8885	A	19990419		
	US 1999-301829	A2	19990429		
	WO 2000-EP2920	A2	20000404		
	GB 2000-25573	A	20001018		
	GB 2000-25574	A	20001018		
	US 2000-690921	A	20001018		
	WO 2001-EP11984	W	20011016		

AB The present invention relates to **adjuvant** compns. which are suitable to be used in vaccines. In particular, the **adjuvant** compn. of the invention comprises a saponin and an **immunostimulatory** oligonucleotide, optionally with a carrier. Also provided by the disclosed invention are vaccines comprising the adjuvants of the present invention and an antigen. Further provided are methods of manuf. of the adjuvants and vaccines of the present invention and their use as medicaments. Methods of treating an individual susceptible to or suffering from a disease by the administration of the vaccines of the present invention are also provided.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 12:06:12 ON 14 AUG 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 12:06:31 ON 14 AUG 2003

E GARCON NATHALIE/AU

L1

57 S E1-E7

L2 E COHEN JOSEPH/AU
 119 S E3
 E VOSS GERALD/AU
 L3 73 S E3
 L4 246 S L1-L3
 L5 8 S L4 AND CPG
 L6 8 DUP REM L5 (0 DUPLICATES REMOVED)
 L7 0 S L4 AND IMMUNOMODULATORY OLIGONUCLEOTIDE
 L8 23 S L4 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP)
 L9 20 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:11:57 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 12:13:03 ON 14 AUG 2003

L10 64 S IMMUNOMODULATORY (5A) OLIGONUCLEOTID?
 L11 31 S L10 AND CPG
 L12 2 S L11 AND (PLASMODIUM OR MALARIA OR RTS OR TRAP)
 L13 12 S L11 AND ANTIGEN
 L14 7 DUP REM L13 (5 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 12:15:39 ON 14 AUG 2003

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 12:15:56 ON 14 AUG 2003

L15 19 DUP REM L11 (12 DUPLICATES REMOVED)
 L16 1286 S CPG AND ADJUVANT
 L17 513 DUP REM L16 (773 DUPLICATES REMOVED)
 L18 216 S L17 AND IMMUNOSTIMULAT?
 L19 19 S L18 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP OR HYBRID)

=> s l18 and phosphorodithioate
 L20 3 L18 AND PHOSPHORODITHIOATE

=> d bib ab 1-3

L20 ANSWER 1 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-493178 [46] WPIDS

DNC C2003-131980

TI **Immunostimulatory** oligonucleotides for use in treating cancer,
 skin disorders, asthma, allergy, comprises two oligonucleotides linked at
 their 3' ends, a nucleobase or sugar by a non-nucleotidic linker.

DC B04 D16

IN AGRAWAL, S; BHAGAT, L; KANDIMALLA, E R; YU, D

PA (HYBR-N) HYBRIDON INC

CYC 89

PI WO 2003035836 A2 20030501 (200346)* EN 96p

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
 RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM
 ZW

ADT WO 2003035836 A2 WO 2002-US33756 20021022

PRAI US 2001-344767P 20011024

AB WO2003035836 A UPAB: 20030719

NOVELTY - An immunomer comprising at least two oligonucleotides linked at
 their 3' ends, or internucleoside linkages or a functionalized nucleobase
 or sugar by a non-nucleotidic linker, where at least one of the
 oligonucleotides is an **immunostimulatory** oligonucleotide having
 an accessible 5' end and comprising an **immunostimulatory**
 dinucleotide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:

(1) an immunomer conjugate comprising the above immunomer, and an antigen conjugated to the immunomer at a position other than the accessible 5' end; and

(2) a pharmaceutical formulation comprising the above immunomer.

ACTIVITY - Cytostatic; Immunosuppressive; Antibacterial; Virucide; Antiparasitic; Antiinflammatory; Antiallergic; Antiasthmatic; Dermatological.

No biological data given.

MECHANISM OF ACTION - Vaccine; Stimulator of immune response.

To test the effect on **immunostimulatory** activity of **CpG** DNA containing branched alkyl-linkers, two branched alkyl-linkers containing a hydroxyl or an amine functional group were incorporated into parent **CpG** DNA (CTATCTGACGTTCTCTGT) and the effects on **immunostimulatory** activity of the resulting modified **CpG** DNAs (CTATCTGCGTTCTCTGT, CTATCTACGTTCTCTGT, CTACTGACGTTCTCTGT) were examined. The data obtained with modified **CpG** DNAs containing aminolinkers at different nucleotide positions, in BALB/c mouse spleen cell cultures (proliferation) and in vivo (splenomegaly) showed that the **CpG** DNA containing an aminobutyryl propanediol-linker induced spleen cell proliferation in BALB/c mice spleen cell cultures and splenomegaly in BALB/c mice. Parent **CpG** DNA showed a proliferation index of 3.7 plus or minus 0.8 at a concentration of 0.1 micro g/ml. At the same concentration, modified **CpG** DNAs containing amino-linker at different positions caused higher spleen cell proliferation than did the parent **CpG** DNA. As observed with other linkers, when the substitution was placed adjacent to **CpG** dinucleotide, a lower proliferation index was noted compared with parent **CpG** DNA, further confirming that the placement of a linker substitution adjacent to **CpG** dinucleotide had a detrimental effect on **immunostimulatory** activity. In general, substitution of an amino-linker for 2'-deoxyribonucleoside in the 5'-flanking sequence resulted in higher spleen cell proliferation than found with the substitution in the 3' flanking sequence. Similar results were observed in the splenomegaly assay, confirming the results observed in spleen cell cultures. Modified **CpG** DNAs containing glycerol-linker showed **immunostimulatory** activity similar to or slightly higher than that observed with modified **CpG** DNA containing an amino-linker.

USE - The immunomer and the immunomer conjugate are useful for generating an immune response in a vertebrate and also for treating a patient having a disease or disorder, such as cancer, autoimmune disorder, airway inflammation, inflammatory disorders, skin disorders, allergy, asthma or a disease caused by a pathogen. The method comprises administering a vaccine, where the vaccine and immunomer are linked to an immunogenic protein, and further administering an **adjuvant** (claimed). The immunomer is useful for treating autoimmune disorders, bacteria, parasitic and viral infections in adult and pediatric human and veterinary applications. The immunomers are also useful as adjuvants in combination with DNA vaccines, antibodies, allergens, chemotherapeutic agents and antisense oligonucleotides.

Dwg.0/21

L20 ANSWER 2 OF 3 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1999-405369 [34] WPIDS
CR 1999-405485 [34]
DNC C1999-119689
TI A vaccine composition for inducing a immune response to T-independent type 1 or type 2 antigen or polysaccharide conjugate antigen.
DC B04 D16
IN DALEMANS, W L J; LAFERRIERE, C A J; PRIEELS, J; GERARD, C M; DALEMANS, W; GERARD, C M G
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 86
PI WO 9933488 A2 19990708 (199934)* EN 35p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
 GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 UA UG US UZ VN YU ZW

AU 9924190 A 19990719 (199951)
 ZA 9811849 A 20000726 (200042) 35p
 EP 1039930 A2 20001004 (200050) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
 NO 2000003303 A 20000804 (200050)
 NO 2000003302 A 20000818 (200052)
 BR 9814483 A 20001010 (200055)
 CZ 2000002375 A3 20001115 (200064)
 CN 1284884 A 20010221 (200131)
 CN 1284885 A 20010221 (200131)
 AU 736099 B 20010726 (200149)
 KR 2001033613 A 20010425 (200164)
 KR 2001033618 A 20010425 (200164)
 MX 2000006323 A1 20010201 (200168)
 MX 2000006324 A1 20010201 (200168)
 JP 2001527050 W 20011225 (200204) 42p
 HU 2001003085 A2 20011128 (200209)
 NZ 505107 A 20030328 (200325)

ADT WO 9933488 A2 WO 1998-EP8562 19981218; AU 9924190 A AU 1999-24190
 19981218; ZA 9811849 A ZA 1998-11849 19981223; EP 1039930 A2 EP
 1998-966705 19981218, WO 1998-EP8562 19981218; NO 2000003303 A WO
 1998-EP8563 19981218, NO 2000-3303 20000623; NO 2000003302 A WO
 1998-EP8562 19981218, NO 2000-3302 20000623; BR 9814483 A BR 1998-14483
 19981218, WO 1998-EP8562 19981218; CZ 2000002375 A3 WO 1998-EP8562
 19981218, CZ 2000-2375 19981218; CN 1284884 A CN 1998-813794 19981218; CN
 1284885 A CN 1998-813795 19981218; AU 736099 B AU 1999-24190 19981218; KR
 2001033613 A KR 2000-707126 20000624; KR 2001033618 A KR 2000-707131
 20000624; MX 2000006323 A1 MX 2000-6323 20000623; MX 2000006324 A1 MX
 2000-6324 20000623; JP 2001527050 W WO 1998-EP8562 19981218, JP
 2000-526239 19981218; HU 2001003085 A2 WO 1998-EP8562 19981218, HU
 2001-3085 19981218; NZ 505107 A NZ 1998-505107 19981218, WO 1998-EP8562
 19981218

FDT AU 9924190 A Based on WO 9933488; EP 1039930 A2 Based on WO 9933488; BR
 9814483 A Based on WO 9933488; CZ 2000002375 A3 Based on WO 9933488; AU
 736099 B Previous Publ. AU 9924190, Based on WO 9933488; JP 2001527050 W
 Based on WO 9933488; HU 2001003085 A2 Based on WO 9933488; NZ 505107 A
 Based on WO 9933488

PRAI GB 1997-27262 19971224

AB WO 9933488 A UPAB: 20030416

NOVELTY - A formulation (A) comprising a CpG oligonucleotide and
 T-independent type 1 or type 2 antigens or polysaccharide conjugate
 antigen, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:

(1) a formulation as in (A), wherein the CpG
 oligonucleotide is selected from the sequences of formula (I)-(IV):
 GCTACTGGTACG TACATTC AGACGGC TCTT (I); ACTATCTAAACGCTAATGGTGCTATGGCGACAG
 GATGGCT (II); TCC ATG ACG TTC CTG ACG TT (III); and TCT CCC AGC GTG CGC
 CAT (IV);

(2) a vaccine composition comprising the formulation, for use in
 medicine; and

(3) a method of inducing an immune response to T independent type 1
 or type 2 antigen or a polysaccharide conjugate antigen, comprising
 administering a safe and effective amount of the formulation to a patient.

USE - The vaccine composition comprising the formulation is used for
 inducing a immune response to T-independent type 1 or type 2 antigen or
 polysaccharide conjugate antigen

ADVANTAGE - The use of **immunostimulatory CpG** oligonucleotide acts as an **adjuvant** to pneumococcal polysaccharides.
Dwg.0/2

L20 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:392056 CAPLUS
DN 135:18544
TI **Immunostimulatory** nucleic acid molecules
IN Krieg, Arthur M.; Kline, Joel N.
PA University of Iowa Research Foundation, USA; Coley Pharmaceutical Group, Inc.; United States Dept. of Health and Human Services
SO U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 738,652.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6239116	B1	20010529	US 1997-960774	19971030
	US 6207646	B1	20010327	US 1996-738652	19961030
	CN 1235609	A	19991117	CN 1997-199352	19971030
	US 6429199	B1	20020806	US 1998-191170	19981113
	KR 2000052994	A	20000825	KR 1999-703873	19990430
	US 2003100527	A1	20030529	US 2002-161229	20020603
PRAI	US 1996-738652	A2	19961030		
	US 1994-276358	B2	19940715		
	US 1995-386063	A1	19950207		
	US 1997-960774	A2	19971030		
	US 1998-191170	A3	19981113		

AB Nucleic acid sequences contg. unmethylated **CpG** dinucleotides that modulate an immune response including stimulating a Th1 pattern of immune activation, cytokine prodn., NK lytic activity, and B cell proliferation are disclosed. The sequences are also useful a synthetic **adjuvant**. The **immunostimulatory** nucleic acids are used for treating tumors, infections, autoimmune diseases, and allergies.

RE.CNT 132 THERE ARE 132 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s immunostimulatory (5a) oligonucleotid?
L21 444 IMMUNOSTIMULATORY (5A) OLIGONUCLEOTID?

=> s l21 and cpG
L22 312 L21 AND CPG

=> s l22 and malaria
L23 7 L22 AND MALARIA

=> s l22 and antigen
L24 152 L22 AND ANTIGEN

=> dup rem l24
PROCESSING COMPLETED FOR L24
L25 82 DUP REM L24 (70 DUPLICATES REMOVED)

=> d bib ab 1-20

L25 ANSWER 1 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1
AN 2003-493178 [46] WPIDS
DNC C2003-131980
TI **Immunostimulatory oligonucleotides** for use in treating cancer, skin disorders, asthma, allergy, comprises two oligonucleotides

linked at their 3' ends, a nucleobase or sugar by a non-nucleotidic linker.

DC B04 D16

IN AGRAWAL, S; BHAGAT, L; KANDIMALLA, E R; YU, D

PA (HYBR-N) HYBRIDON INC

CYC 89

PI WO 2003035836 A2 20030501 (200346)* EN 96p

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM
ZW

ADT WO 2003035836 A2 WO 2002-US33756 20021022

PRAI US 2001-344767P 20011024

AB WO2003035836 A UPAB: 20030719

NOVELTY - An immunomer comprising at least two oligonucleotides linked at their 3' ends, or internucleoside linkages or a functionalized nucleobase or sugar by a non-nucleotidic linker, where at least one of the **oligonucleotides** is an **immunostimulatory oligonucleotide** having an accessible 5' end and comprising an immunostimulatory dinucleotide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an immunomer conjugate comprising the above immunomer, and an **antigen** conjugated to the immunomer at a position other than the accessible 5' end; and

(2) a pharmaceutical formulation comprising the above immunomer.

ACTIVITY - Cytostatic; Immunosuppressive; Antibacterial; Virucide; Antiparasitic; Antiinflammatory; Antiallergic; Antiasthmatic; Dermatological.

No biological data given.

MECHANISM OF ACTION - Vaccine; Stimulator of immune response.

To test the effect on immunostimulatory activity of **CpG** DNA containing branched alkyl-linkers, two branched alkyl-linkers containing a hydroxyl or an amine functional group were incorporated into parent **CpG** DNA (CTATCTGACGTTCTCTGT) and the effects on immunostimulatory activity of the resulting modified **CpG** DNAs (CTATCTGCGTTCTCTGT, CTATCTACGTTCTCTGT, CTA CTGACGTTCTCTGT) were examined. The data obtained with modified **CpG** DNAs containing aminolinkers at different nucleotide positions, in BALB/c mouse spleen cell cultures (proliferation) and in vivo (splenomegaly) showed that the **CpG** DNA containing an aminobutyryl propanediol-linker induced spleen cell proliferation in BALB/c mice spleen cell cultures and splenomegaly in BALB/c mice. Parent **CpG** DNA showed a proliferation index of 3.7 plus or minus 0.8 at a concentration of 0.1 micro g/ml. At the same concentration, modified **CpG** DNAs containing amino-linker at different positions caused higher spleen cell proliferation than did the parent **CpG** DNA. As observed with other linkers, when the substitution was placed adjacent to **CpG** dinucleotide, a lower proliferation index was noted compared with parent **CpG** DNA, further confirming that the placement of a linker substitution adjacent to **CpG** dinucleotide had a detrimental effect on immunostimulatory activity. In general, substitution of an amino-linker for 2'-deoxyribonucleoside in the 5'-flanking sequence resulted in higher spleen cell proliferation than found with the substitution in the 3' flanking sequence. Similar results were observed in the splenomegaly assay, confirming the results observed in spleen cell cultures. Modified **CpG** DNAs containing glycerol-linker showed immunostimulatory activity similar to or slightly higher than that observed with modified **CpG** DNA containing an amino-linker.

USE - The immunomer and the immunomer conjugate are useful for generating an immune response in a vertebrate and also for treating a patient having a disease or disorder, such as cancer, autoimmune disorder, airway inflammation, inflammatory disorders, skin disorders, allergy,

asthma or a disease caused by a pathogen. The method comprises administering a vaccine, where the vaccine and immunomer are linked to an immunogenic protein, and further administering an adjuvant (claimed). The immunomer is useful for treating autoimmune disorders, bacteria, parasitic and viral infections in adult and pediatric human and veterinary applications. The immunomers are also useful as adjuvants in combination with DNA vaccines, antibodies, allergens, chemotherapeutic agents and antisense oligonucleotides.

Dwg.0/21

L25 ANSWER 2 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 2
AN 2003-354564 [33] WPIDS
DNC C2003-093465
TI New compositions comprising immunostimulatory substances packaged into virus-like particles, useful as a vaccine for enhancing an immune response in animals, e.g. for treating or preventing allergies, tumors or viral infections.
DC B04 D16
IN BACHMANN, M; CIELENS, I; LIPOWSKY, G; MAURER, P; MEIJERINK, E; PUMPENS, P; RENHOFA, R; SCHWARZ, K; STORNI, T; TISSOT, A; BACHMANN, M F
PA (CIEL-I) CIELENS I; (CYTO-N) CYTOS BIOTECHNOLOGY AG; (LIPO-I) LIPOWSKY G; (MAUR-I) MAURER P; (MEIJ-I) MEIJERINK E; (PUMP-I) PUMPENS P; (RENH-I) RENHOFA R; (SCHW-I) SCHWARZ K; (TISS-I) TISSOT A
CYC 101
PI WO 2003024481 A2 20030327 (200333)* EN 322p
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
ZM ZW
US 2003099668 A1 20030529 (200337)
ADT WO 2003024481 A2 WO 2002-IB4132 20020916; US 2003099668 A1 Provisional US 2001-318994P 20010914, Provisional US 2002-374145P 20020422, US 2002-244065 20020916
PRAI US 2002-374145P 20020422; US 2001-318994P 20010914; US 2002-244065 20020916
AB WO2003024481 A UPAB: 20030526
NOVELTY - A composition for enhancing immune response in animal comprising a virus-like particle, and an immunostimulatory substance, is new. The immunostimulatory substance is bound to the virus-particle particle.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) enhancing an immune response in an animal by introducing into the animal the new composition;
(2) producing the composition for enhancing an immune response in an animal;
(3) vaccines comprising the new composition together with a pharmaceutical diluent, carrier or excipient; and
(4) immunizing or treating an animal by:
(a) administering the vaccine to the animal;
(b) priming a T cell response in the animal by administering the vaccine; or
(c) boosting a T cell response in the animal by administering the vaccine.
ACTIVITY - Immunostimulant; Cytostatic; Antiallergic; Virucide; Antibacterial.
Mice were subcutaneously primed with 100 micro g p33-VLP alone, mixed with 20 nmol CpG-oligonucleotide (p33-VLP+CpG), or p33-VLP packaged with CpG-oligonucleotide after dialysis of free CpG-oligonucleotide (p33-VLP/CpG). Untreated naive mice served as negative control. Twenty days later, mice were challenged with lymphocytic choriomeningitis virus (LCMV) (200 plaque forming units

(pfu), intravenously). Results showed that LCMV titer (log10) was lowest for p33-VLP/CpG.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful as a vaccine for enhancing an immune response in an animal, particularly a mammal or human. Specifically, the composition is useful for enhancing a B cell response, a T cell response (particularly a Th or Th1 cell response), or a cytotoxic T-lymphocyte (CTL) response. (All claimed.) The composition or vaccine is also useful for immunizing or treating an animal (claimed), e.g. humans, sheep, horses, cattle, pigs, dogs, cats, rats, birds, reptiles or fish. The composition is particularly useful as prophylactic or therapeutic vaccines against allergies, tumors (e.g. breast cancers, neuroblastoma, or leukemia), viral diseases (e.g. influenza, hepatitis, measles or chicken pox), or bacterial infections (e.g. tuberculosis, pneumonia or syphilis).
Dwg.0/55

L25 ANSWER 3 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 3
AN 2003-363095 [34] WPIDS
DNC C2003-095845

TI A composition, useful for enhancing an immune response against an **antigen** or a virus-like particle, enhancing anti-viral protection in an animal, or immunizing or treating tumors or infectious diseases, e.g. viral infections.

DC B04 D16

IN BACHMANN, M F; LECHNER, F; STORNI, T

PA (CYTO-N) CYTOS BIOTECHNOLOGY AG

CYC 101

PI WO 2003024480 A2 20030327 (200334)* EN 243p

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
ZM ZW

US 2003091593 A1 20030515 (200335)

ADT WO 2003024480 A2 WO 2002-IB4252 20020916; US 2003091593 A1 Provisional US
2001-318967P 20010914, US 2002-243739 20020916

PRAI US 2001-318967P 20010914; US 2002-243739 20020916

AB WO2003024480 A UPAB: 20030529

NOVELTY - A composition for enhancing an immune response against an **antigen** or a virus-like particle in an animal comprising a virus-like particle bound to at least one **antigen**, or a virus-like particle capable of being recognized by the immune system of the animal, is new.

DETAILED DESCRIPTION - A composition for enhancing an immune response against an **antigen** or a virus-like particle in an animal comprising a virus-like particle bound to at least one **antigen**, or a virus-like particle capable of being recognized by the immune system of the animal, and capable of inducing an immune response against the **antigen** or the virus-like particle in the animal, and at least one substance that activates **antigen** presenting cells to enhance the immune response of the animal to the **antigen** or the virus-like particle, is new.

INDEPENDENT CLAIMS are also included for:

(1) enhancing an immune response against an **antigen** or a virus-like particle in an animal comprising introducing into the animal the composition cited above;

(2) vaccines comprising the novel composition together with a pharmaceutical diluent, carrier or excipient;

(3) immunizing or treating an animal comprising administering the vaccine to the animal, or priming or boosting a T cell response in the animal by administering the vaccine; and

(4) enhancing anti-viral protection in an animal comprising introducing the composition into the animal.

ACTIVITY - Cytostatic; Virucide; Antibacterial; Antiparasitic; Fungicide; Antiallergic; Immunosuppressive; Antiaddictive; Antiinflammatory; Antithyroid; Antidiabetic; Neuroprotective; Nootropic; Osteopathic; Antirheumatic; Antiarthritic.

No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The compositions or vaccines are useful for enhancing an immune response against an **antigen** or a virus-like particle in an animal, enhancing anti-viral protection in an animal, or immunizing or treating tumors and infectious diseases such as viral, bacterial, parasitic or fungal infections. The vaccine compositions are also useful for preventing or treating allergies, drug addiction, graft-versus-host disease, Crohn's disease, Grave's disease, diabetes, multiple sclerosis, Alzheimer's disease, osteoporosis, rheumatoid arthritis, or inflammatory autoimmune disease.

Dwg.0/20

L25 ANSWER 4 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-381683 [36] WPIDS

DNC C2003-101434

TI New compositions comprising an immunostimulatory nucleic acid and an oil-in-water emulsion, useful for reducing viral shedding or tissue damage upon vaccination, or for inducing an immune response against infectious diseases.

DC B04 C06 D16

IN BABIUK, L A; HECKER, R

PA (QIAG-N) QIAGEN GMBH; (UYSA-N) UNIV SASKATCHEWAN

CYC 100

PI WO 2003030934 A2 20030417 (200336)* EN 34p

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW

ADT WO 2003030934 A2 WO 2002-EP11206 20021007

PRAI US 2001-327734P 20011006

AB WO2003030934 A UPAB: 20030609

NOVELTY - A composition comprising an immunostimulatory nucleic acid and an oil-in-water emulsion, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) reducing viral shedding in a non-human animal by administering to a non-human animal infected with virus or at risk of viral infection, an immunostimulatory nucleic acid and an oil-in-water emulsion;

(2) reducing tissue damage upon vaccination of a subject by administering to a subject by an invasive route an adjuvanted vaccine and an immunostimulatory nucleic acid to reduce tissue damage arising from the adjuvanted vaccine, where the vaccine is adjuvanted with an oil-in-water emulsion;

(3) inducing an immune response by administering to a subject an oil-in-water emulsion and a **CpG** oligonucleotide to produce the immune response; and

(4) reducing a dosage of **antigen** administered to a subject to produce an **antigen** specific immune response comprising administering to a subject an **antigen** in a sub-therapeutic dosage and an immunostimulatory nucleic acid.

ACTIVITY - Virucide; Immunostimulant; Cytostatic; Antibacterial; Fungicide.

Eight groups of seven 9-month old bovine hepatitis virus (BHV)-1-seronegative Angus and Hereford cross calves were immunized

subcutaneously with 50 micro g BHV-1 tgD adjuvanted with either 30% vol/vol EMULSIGEN (Em), 30% vol/vol VSA3, 25 mg of **CpG** ODN (**CpG**), a combination of 30% Em and 25 (high), 2.5 (medium) or 0.25 (low) mg **CpG** ODN, or with a combination of Em and 25 mg non-**CpG** ODN. Vaccines were administered subcutaneously. A placebo group of calves was immunized with PBS only. After 39 days, animals were re-immunized and challenged 2 weeks after the secondary immunization. Five weeks after secondary immunization, animals were transported into an isolated pen, weighed, examined clinically, and individually exposed for 4 minutes to an aerosol of 107 plaque forming units (PFU) of BHV-1. Following challenge, calves were weighed daily and clinically evaluated for 11 consecutive days. Specific antibody responses were determined before and after challenge using enzyme linked immunosorbant assay (ELISA), and the extent of shedding from the nasal passages was assessed. With the exception of VSA3 group, all vaccinated groups had significantly higher levels of neutralizing antibodies than the placebo group after 14 days following primary immunization. Antibody levels in the H-**CpG**/Em group were significantly higher than those of the non-**CpG**/Em, Em **CpG** or VSA3 groups. Animals in the **CpG**, Em and non-**CpG**/Em groups began shedding virus on day 2 after challenge and continued to do so at least until day 8, and no virus was recovered from the nasal tampons of animals in either of the **CpG**/Em groups.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful for reducing viral shedding in a non-human animal infected with a virus or at risk of viral infection, for reducing tissue damage upon vaccination, for inducing an immune response to treat or prevent infectious diseases, for reducing a dosage of **antigen** administered to a subject to produce an **antigen** specific immune response, and for treating or preventing cancer (e.g. bone cancer, brain and CNS cancer, connective tissue cancer, esophageal cancer, eye cancer, Hodgkin's lymphoma, larynx cancer, oral cavity cancer, skin cancer, or testicular cancer), bacterial, viral and fungal infections.

L25 ANSWER 5 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2003-381666 [36] WPIDS

DNC C2003-101417

TI Inducing weight growth and innate immunity in young animals, including neonates for e.g. chickens, involves administering immunostimulatory nucleic acids.

DC B04 C06 D13 D16

IN BABIUK, L A; GOMIS, S; GRIEBEL, P J; HECKER, R; POTTER, A A

PA (QIAG-N) QIAGEN GMBH; (UYSA-N) UNIV SASKATCHEWAN

CYC 100

PI WO 2003030656 A2 20030417 (200336)* EN 60p

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW

ADT WO 2003030656 A2 WO 2002-EP11212 20021007

PRAI US 2001-327703P 20011006

AB WO2003030656 A UPAB: 20030609

NOVELTY - Increasing (M) the rate of growth of feed animals, and promoting innate immunity in a young non-human or in a non-human animal in utero, comprises administering an immunostimulatory nucleic acid (ISN). For promoting innate immunity, ISN is administered without the co-administration of an **antigen** to induce innate immunity.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition (C) comprising an ISN formulated for oral or subcutaneous administration to a feed animal.

ACTIVITY - None given.

MECHANISM OF ACTION - Inducer of innate immunity.

Chickens at 22 days of age were administered **CpG** ISN (TCGTCGTTGTCGTTTGTGCGTT) either intramuscularly (in the leg) or subcutaneously (in the abdominal area). **CpG** nucleic acids were administered in either low dose (i.e. 10 micro g/bird) or high dose (50 micro g/bird). Three days later, the chickens were actively exposed to *Escherichia coli* by making a 2 cm scratch on the caudal abdominal area and swabbing the scratched area with an *E. coli* carrying swab. Control chickens did not receive any **CpG** nucleic acid, but they were exposed to *E. coli* (virulent isolate strain EC317). Each group ranged in number from 20-40 birds depending upon the experiment. Chickens were examined for 10 days post *E. coli* challenge. Clinical scores were evaluated daily and chickens meeting a predetermined criteria were euthanized. Parameters measured included body weight at the time of nucleic acid administration, at the time of *E. coli* challenge, and at the time of necropsy. Pathological and bacteriological assessments were conducted on all dead or euthanized animals, including all the remaining birds at the termination of the trial on day 10 post-infection with *E. coli*.

In some experiments, dose titrations were performed using **CpG** ISNs in absolute doses of 100 micro g/bird, 31.6 micro g/bird, 10 micro g/bird and 3.16 micro g/bird. In addition, a control **oligonucleotide** that lacked any identifiable **immunostimulatory** motif was administered to control animals. **CpG** ISN was also administered at a dose of 31.6 micro g/bird to the neck area in other chickens. The control group of birds that received no **CpG** nucleic acid had a survival rate of 15%. In contrast, groups that received **CpG** nucleic acid by subcutaneous or intramuscular injection had significantly higher survival rates.

Accordingly, mortality was significantly reduced in all groups receiving **CpG** nucleic acids compared to control. The size of the lesions at the site of infection of *E. coli* was significantly smaller in groups that received **CpG** nucleic acids by subcutaneous route as compared to groups that did not receive **CpG** nucleic acids and those that received **CpG** by intramuscular injection. Injection of **CpG** nucleic acids intramuscularly or subcutaneously in the neck was less effective at inducing local and systemic innate immunity in chickens as compared to injection of **CpG** nucleic acids directly to the site of initial infection.

These data demonstrated the efficacy of **CpG** nucleic acid as an immunostimulant in a young non-human animal.

USE - (M) is useful for increasing rate of growth of feed animals, such as chicken. The feed animal was born prematurely, and is a multiple delivery animal. (M) is also useful for promoting innate immunity in a young non-human animal such as chicken or in a non-human animal in utero (claimed).

The feed animals may also include pigs, buffalo, cows, ducks, pigeons, turkeys, geese, rabbits, deer, goats, sheep, quail, bison, horse, moose and shellfish such as shrimp, lobster, clams, oysters and mussels. ISN can also be administered for promoting the growth of laboratory animals such as mice and rats.

ADVANTAGE - The time required for chicken to reach acceptable size for feed is reduced by one day compared to a chicken that is not administered the ISN (claimed).

Dwg.0/14

L25 ANSWER 6 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:434399 CAPLUS
DN 139:21040
TI Methods for treating cancer
IN Vicari, Alain P.; Caux, Christophe
PA Schering Corporation, USA

SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003045431	A2	20030605	WO 2002-US38098	20021126
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2003138413 A1 20030724 US 2002-304616 20021126

PRAI US 2001-333434P P 20011127

AB Dendritic cells (DC) play a crit. role in **antigen**-specific immune responses. The authors disclose materials and methods for treating disease states, including cancer, by activating dendritic cells from the host which are rendered hypo-responsive to activation stimuli by the disease. In particular, methods are provided for treating cancer in a mammal comprising administering to said mammal an effective amt. of a tumor-derived DC inhibitory factor antagonist (e.g., anti-interleukin-10 receptor) in combination with an effective amt. of a Toll-like receptor (TLR) agonist.

L25 ANSWER 7 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:242434 CAPLUS

DN 138:253711

TI Compositions comprising **immunostimulatory oligonucleotides** and uses thereof to enhance Fc receptor-mediated immunotherapies

IN Van de Winkel, Jan G. J.

PA Medarex, Inc., USA

SO PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003025119	A2	20030327	WO 2002-US24154	20020730
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2003072762 A1 20030417 US 2002-209070 20020730

PRAI US 2001-310437P P 20010803

AB Comps. comprising **immunostimulatory oligonucleotides** (CpGODN) and FcR-directed immunotherapeutics are disclosed. Also disclosed are methods of using the comps. to enhance FcR-mediated **antigen** presentation, ADCC, and other FcR-mediated immune responses.

L25 ANSWER 8 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2003:570637 CAPLUS
 TI Methods and products for enhancing immune responses using imidazoquinoline compounds in combination with modified **immunostimulatory oligonucleotide**
 IN Krieg, Arthur M.; Schetter, Christian; Bratzler, Robert L.; Vollmer, Jorg; Jurk, Marion; Bauer, Stefan
 PA University of Iowa Research Foundation, USA
 SO U.S. Pat. Appl. Publ., 112 pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003139364	A1	20030724	US 2002-272502	20021015
PRAI	US 2001-329208P	P	20011012		

AB The invention involves administration of an imidazoquinoline agent in combination with another therapeutic agent. The combination of drugs may be administered in synergistic amts. or in various dosages or at various time schedules. The invention also relates to kits and compns. concerning the combination of drugs. The combinations can be used to enhance ADCC, stimulate immune responses and/or patient and treat certain disorders. Specifically, the imidazoquinoline compns. R-848 is used which is shown to be more potent inducer of proinflammatory cytokines NF- κ B in 293T cells by reconstitution of TLR9 signaling through co-transfecting TLR9, TLR8 and TLR7 into 293T cell. Furthermore, **CpG** oligonucleotides (ODNs, in particular, **CpG** ODN #7909) and R-848 are tested either together or individually for their ability to augment a cytolytic T lymphocyte response against **antigen** (e.g., HBsAg) in vivo using mouse model. The combination of R-848 and **CpG** ODN together is shown to result in an additive effect; while no augmentation of the CTL response over **antigen** alone is obsd. using control ODN either alone or with R-848. The distribution of antibody isotype also shows **CpG** ODN produces higher levels of IgG2a antibodies regardless of whether R-848 is present, and R-848 appears to increase the level of IgG2a and decrease the level of IgG1 as compared to the **antigen** alone response.

L25 ANSWER 9 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2003:276663 CAPLUS
 DN 138:302632
 TI Adjuvant compns. and uses thereof in vaccines
 IN Friede, Martin; Garcon, Nathalie; Gerard, Catherine Marie Ghislaine; Hermand, Philippe
 PA Smithkline Beecham Biologicals S.A., Belg.
 SO U.S., 29 pp., Cont.-in-part of Appl. No. PCT/EP00/02920.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6544518	B1	20030408	US 2000-690921	20001018
	US 6558670	B1	20030506	US 1999-301829	19990429
	WO 2000062800	A2	20001026	WO 2000-EP2920	20000404
	WO 2000062800	A3	20010111		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,

helminth-infection related disorders, fibrosis or cirrhosis of the liver.

DC B04 D16

IN ASHMAN, C; CROWE, J S; ELLIS, J H; LEWIS, A P

PA (GLAX) GLAXO GROUP LTD

CYC 100

PI WO 2002070711 A1 20020912 (200280)* EN 83p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW

ADT WO 2002070711 A1 WO 2002-GB900 20020301

PRAI GB 2001-5360 20010303

AB WO 2002070711 A UPAB: 20021212

NOVELTY - A new isolated protein at least 30% identical to a human protein comprising a polypeptide, which:

(a) contains at least one mutation characteristic of an analogous non-human protein;

(b) is capable of raising antibodies in human and is sufficiently structurally similar to the human protein that the antibodies bind to both the human protein and the polypeptide; and

(c) is not an antibody.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a protein having B-cell epitopes from a mammalian self **antigen** and a mutation that gives rise to a sequence of an analogous protein of a second mammalian species (the protein is able to raise in the species from which the B-cell epitopes derived, an immune response that recognizes the natural protein from which the B-cell epitopes are derived);

(2) a protein having B-cell epitopes of cell protein, which are grafted by substitution, into a framework of an analogous protein from a second mammalian species (the protein is able to raise in the species from which the B-cell epitopes derived, an immune response that recognizes the natural protein from which the B-cell epitopes are derived);

(3) a mutated human-interleukin-13 (IL-13) having one or more of the following substitutions or conservative substitutions:

(a) R to K at position 30;

(b) V to S at position 37;

(c) Y to F at position 63;

(d) A to V at position 65;

(e) E to D at position 68;

(f) E to Y at position 80;

(g) K to R at position 81;

(h) M to I at position 85;

(i) G to H at position 87;

(j) Q to H at position 113; (k) V to I at position 115; or (l) D to K at position 117;

(4) a mutated human gIL-13 comprising 111 amino acids, fully defined in the specification;

(5) a polynucleotide encoding any of the proteins cited above;

(6) a vector comprising the polynucleotide in (5);

(7) a host cell transformed with the polynucleotide or vector cited above;

(8) a pharmaceutical composition comprising the protein, polynucleotide, vector cited above, and a carrier or excipient;

(9) a method for the treatment or prophylaxis of IL-13 mediated disease comprising administration of the composition in (8) in patient; and

(10) a method for preparing the protein.

ACTIVITY - Antiinflammatory; Antiasthmatic; Antiallergic; Anthelmintic; Vulnerary; Cytostatic; Hepatotropic.

MECHANISM OF ACTION - Vaccine; Gene therapy.

Female mice aged 6-8 weeks were given one subcutaneous injection of approximately 30 psi g protein in complete Freund's adjuvant (CFA) at the base of the tail. This was followed by three booster immunizations at the same site, each consisting of approximately 10 micro g protein in incomplete Freund's adjuvant for boosts. Serum samples were obtained by venepuncture of the tail vein. After clarification by centrifugation, the samples were assayed by enzyme linked immunosorbent assay (ELISA) for the presence of immunoglobulin (Ig) G responses to mouse IL-13, human IL-13 and GST. The results indicate that immunization with GST-cIL-13 or cIL-13 was able to break tolerance to mIL-13, generating mouse anti-mIL-13 antibodies.

USE - The proteins, polynucleotides, vectors, hosts and compositions are useful in medicine for the treatment of IL-13 mediated diseases, such as asthma (claimed), chronic obstructive pulmonary disease (COPD), or allergies. The polypeptides or the polynucleotides are useful for the treating helminth-infection related disorders, fibrosis or cirrhosis of the liver.

Dwg. 0/13

L25 ANSWER 16 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 9
AN 2002-557504 [59] WPIDS
DNC C2002-158200
TI CYP1B1 polynucleotide for inducing immune response against cancer, has transcriptional units encoding polypeptides, and lack sequences found in untranslated region of naturally occurring forms of transcript.
DC B04 D16
IN AZIZ, N; COLE, G; HEDLEY, M L; TOMLINSON, A J; URBAN, R G
PA (ZYCO-N) ZYCOS INC; (AZIZ-I) AZIZ N; (COLE-I) COLE G; (HEDL-I) HEDLEY M L; (TOML-I) TOMLINSON A J; (URBA-I) URBAN R G
CYC 96
PI WO 2002042325 A2 20020530 (200259)* EN 73p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002039410 A 20020603 (200263)
US 2003028000 A1 20030206 (200313)
ADT WO 2002042325 A2 WO 2001-US45170 20011031; AU 2002039410 A AU 2002-39410
20011031; US 2003028000 A1 Provisional US 2000-244501P 20001031,
Provisional US 2001-261719P 20010112, Provisional US 2001-298428P
20010615, US 2001-999686 20011031
FDT AU 2002039410 A Based on WO 200242325
PRAI US 2001-298428P 20010615; US 2000-244501P 20001031; US 2001-261719P
20010112; US 2001-999686 20011031
AB WO 200242325 A UPAB: 20020916
NOVELTY - A polynucleotide (I) comprising a transcriptional unit (TU),
having sequence encoding CYP1B1, or protein comprising a peptide that
binds to a major histocompatibility complex class I or II molecule, where
TU does not contain translational repressor element operably linked to
coding sequence or 150 consecutive nucleotides of sequence of 1-362 or
2011-5128 of 5110 base pairs sequence as given in specification, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
following:
(1) polynucleotide (II) comprising a TU encoding a hybrid polypeptide
which comprises a first and a second segment of CYP1B1, which are either
contiguous or separated by a spacer amino acid or spacer peptide, where
the two segments are each at least eight amino acids in length, and are
non-contiguous portions of CYP1B1;
(2) a composition (C1) comprising (I), and an immunostimulatory agent
or nucleic acid encoding the agent;

- (3) a therapeutic composition (C2) comprising (I) and a carrier; and
(4) a microparticle (MP) comprising a polymeric matrix or shell and
(I).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - T or B cell response inducer. (claimed). Three strains of mice (C3H, C57/B16 and Balb/c) were injected (intramuscularly) with 100 micro g of pcDNA3-hulB1, which encodes a protein that is processed, presented and can stimulate major histocompatibility complex (MHC) class II CD4+ T cell response. Mice were boosted on day 14 with the same dose of pcDNA3-hulB1. Spleens were harvested on day 27 and IFN-g ELISPOT assays were performed using CD4+T cell enriched splenocytes tested against syngeneic **antigen** presenting cell (APC) pulsed with peptide. In addition, CD4+T cells isolated from naive mice were screened to serve as a negative control. All CD4+T cells were screened against a panel of synthetic CYP1B1 30 mer peptides, phytohemagglutinin (PHA), and hepatitis B virus (HBV)-2. The results of the above assay showed that CYP1B1 peptides stimulated a response in each of the three mouse strains tested. All reported values represent IFN-g Spot Forming Cells (SFC)/1,000,000 CD4+T cells.

USE - (I) or MP is useful for inducing an immune response especially T or B cell response, in a mammal suffering from or is at risk for cancer, where the method preferably comprises detecting expression of CYP1B1 in a tumor of a mammal, and administering (I), where the mammal belongs to a species especially human, and CYP1B1 or its portion is identical to a sequence of a naturally occurring CYP1B1 polypeptide of a different species which is a rodent preferably a rat or mouse. (I) is further useful for reducing tumor growth or tumor activity in a mammal by identifying a mammal having a tumor, administering (I), and detecting a reduction in the size or activity of the tumor (claimed).

Dwg.0/9

L25 ANSWER 17 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 10
AN 2002-499992 [53] WPIDS
DNC C2002-141547

TI Adjuvant composition useful in vaccine composition for use in medicine,
comprises combination of **immunostimulatory**
oligonucleotide and tocol.

DC B02 B04 D16

IN GARCON, N; GERARD, C M G; STEPHENNE, J

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS
SA

CYC 98

PI WO 2002032454 A1 20020425 (200253)* EN 42p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002021689 A 20020429 (200255)

EP 1326639 A1 20030716 (200347) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

NO 2003001646 A 20030614 (200351)

ADT WO 2002032454 A1 WO 2001-EP11985 20011016; AU 2002021689 A AU 2002-21689
20011016; EP 1326639 A1 EP 2001-987673 20011016, WO 2001-EP11985 20011016;
NO 2003001646 A WO 2001-EP11985 20011016, NO 2003-1646 20030410

FDT AU 2002021689 A Based on WO 200232454; EP 1326639 A1 Based on WO 200232454

PRAI GB 2000-25577 20001018

AB WO 200232454 A UPAB: 20020820

NOVELTY - An adjuvant composition (I) comprising a combination of an
immunostimulatory oligonucleotide (Ia) and a tocol (Ib),
is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a vaccine composition (II) comprising (I), and an **antigen** or antigenic composition;
- (2) shifting (M1) the quality of an immune response against an **antigen**, generated by a vaccine comprising an **immunostimulatory oligonucleotide**, towards a Th1-type immune response, by formulating the vaccine with (Ia) and (Ib); and
- (3) manufacturing a vaccine formulation, by formulating an oil in water emulsion comprising a tocol, admixing the tocol emulsion with an **immunostimulatory oligonucleotide** to form an adjuvant, and formulating the adjuvant with an **antigen** or antigenic composition.

ACTIVITY - Antiallergic; Antibacterial; Antifungal; Virucide; Cytostatic; Antiarteriosclerotic; Nootropic; Neuroprotective; Anti-HIV; Tuberculostatic; Hepatotropic.

MECHANISM OF ACTION - Vaccine (claimed). A range of adjuvant formulations with **antigen** (a fusion of the extracellular domain of Her2Neu linked to the phosphorylation domain (ECD-PD) were investigated. Groups 1-11 were treated with adjuvant formulations comprising the following 11 adjuvants and 25 micro g of **antigen**. The adjuvants include phosphate buffered saline (PBS); liposomes with QS21 and 3D-MPL in membrane; tocol containing oil in water emulsion with QS21 and 3D-MPL; **CpG**; liposomes with QS21 and 3D-MPL in membrane + **CpG**; tocol containing oil in water emulsion with QS21 and 3D-MPL + **CpG**; 3D-MPL + **CpG**; QS21 + **CpG**; tocol containing oil in water emulsion + **CpG**; liposomes with QS21 in membrane + **CpG**; and liposomes with 3D-MPL in membrane + **CpG**. Groups of B6F1 mice were vaccinated on four occasions, intramuscularly, 14 days apart. Fourteen days post the 4th vaccine dose, the mice were challenged subcutaneously with 2 multiply 10 to the power of 6 TC1 tumor cell expressing the Her2Neu. The size of the individual tumors were measured twice a week and expressed as a group mean. The results were shown graphically. Formulations comprising tocol and **CpG** induced a complete regression of the tumor.

USE - (II) is useful for treating an individual susceptible to or suffering from a disease, and in medicine (claimed). (I) is useful in vaccine. (I) is useful for immunoprophylaxis of diseases, and also for immunotherapy of diseases such as persistent viral, bacterial or parasitic infections, or chronic disorders, such as cancer. (II) is useful in prophylaxis or therapy of allergy, chronic disorders or diseases such as atherosclerosis and Alzheimer's disease, and persistent infections. (II) is particularly suitable for the immunotherapy of infectious diseases such as tuberculosis, AIDS and hepatitis B virus infections.

Dwg.0/10

L25 ANSWER 18 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 11
AN 2002-471376 [50] WPIDS
CR 2000-687101 [67]
DNC C2002-134015
TI Immunogenic composition useful for treating patients suffering from cancer comprising cancer antigens e.g., MAGE, prostate, along with adjuvant combination comprising **immunostimulatory oligonucleotide** and saponin.
DC B04 D16
IN GARCON, N; GERARD, C M G; STEPHENNE, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS
SA
CYC 98
PI WO 2002032450 A2 20020425 (200250)* EN 49p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002044337 A 20020429 (200255)
EP 1326638 A2 20030716 (200347) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

NO 2003001705 A 20030614 (200351)

ADT WO 2002032450 A2 WO 2001-EP11984 20011016; AU 2002044337 A AU 2002-44337
20011016; EP 1326638 A2 EP 2001-987671 20011016, WO 2001-EP11984 20011016;
NO 2003001705 A WO 2001-EP11984 20011016, NO 2003-1705 20030411

FDT AU 2002044337 A Based on WO 200232450; EP 1326638 A2 Based on WO 200232450
PRAI US 2000-690921 20001018; GB 2000-25573 20001018; GB 2000-25574

20001018

AB WO 200232450 A UPAB: 20030808

NOVELTY - New Immunogenic composition (I) comprises:

(a) a cancer **antigen** (CA) e.g. MAGE or prostate antigens
linked to heterologous fusion partner, prostate fragments comprising at
least 20 amino acids of prostate, mutated prostate, P501S, Cripto, or
Her2-neu derivatives devoid of substantial portion of Her-2 neu
transmembrane domain, and

(b) adjuvant comprising saponin and **immunostimulatory
oligonucleotide**.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use
of a combination of a saponin and **immunostimulatory
oligonucleotide** and a CA in the manufacture of a medicament for
the treatment or prophylaxis of tumors.

ACTIVITY - Cytostatic; antimicrobial; antiallergic;
immunosuppressive.

MECHANISM OF ACTION - Vaccine.

A range of adjuvant formulations with the **antigen** which was
a fusion of the extracellular domain of Her 2 neu linked to the
phosphorylation domain (ECD-PD) (ECD-PD with no adjuvant (group 1) and
ECD-PD with liposomes with QS21 and with any of the adjuvant combinations
3D-MPL in membrane, tocol containing oil in water emulsion with QS21 and
3D-MPL **CpG**, liposomes with QS21 and 3D-MPL in membrane +
CpG, tocol containing oil in water emulsion with QS21 and 3D-MPL+
CpG, 3D-MPL+**CpG**, QS21+**CpG**, tocol containing
oil in water emulsion+**CpG**, liposomes with QS21 in membrane+
CpG, liposomes with 3D-MPL in membrane+**CpG** (groups 2-11,
respectively)) which was produced in Chinese hamster ovary (CHO) cells
according to the methods of WO 00/44899, was investigated. Groups of B6F1
mice were vaccinated on four occasions (in 50 μ l volumes),
intramuscularly, 14 days apart. 14 days post the 4th vaccine dose, the
mice were challenged subcutaneously with 2×10^6 TC1 tumor cell expressing
the Her 2 neu. The Her 2 neu-TC1 tumor cell lines was produced by
transduction of TC1 cells by retroviral vectors coding for Her 2 neu.
After a selection period with blastocystin, resistant clones were isolated
and screened by fluorescence activated cell sorting (FACS) for Her 2 neu
expression. The clone with the highest Her 2 neu expression was selected,
and the challenge dose of 2×10^6 was identified to have a similar kinetic
of growth as the wild-type TC1 cells and to give rise to a developing
tumor in 100% of the control animals. The only vaccines that induced a
complete regression of the tumor were vaccine containing both an
immunostimulatory oligonucleotide and a saponin. The
adjuvant tested (AS1, AS2, AS7) had similar effect. However, the
combination of AS1 and AS7 or AS2 and AS7 were more effective adjuvants.
Cell-mediated immune response (CMI) was clearly shown after 4 vaccinations
in animals receiving the combined adjuvant on the whole molecule ECD-PD,
but also on each part separately (ECD and ICD). The formulations were very
effective in inducing tumor regression.

USE - (I) is useful for treating a patient suffering from susceptible
to a cancer expressing a Her 2 neu or prostate specific/tumor
antigen. (I) is also useful for treating a patient suffering from

or susceptible to a cancer expressing any of MAGE, prostate, P501S or Cripto (claimed).

The formulations containing tumor antigens are useful for immunotherapeutic treatment of prostate, breast, colorectal, lung, pancreatic, renal, or melanoma cancers. (I) is useful for inducing an immune response in an individual, and for treating a mammal susceptible to or suffering from an infectious disease or cancer, or allergy or autoimmune disease. (I) is useful as a medicament.

ADVANTAGE - The **immunostimulatory oligonucleotides** (**CpG**) and saponin and optionally a lipopolysaccharide combination are extremely potent adjuvants. The oligonucleotides in the adjuvant and vaccine compositions act synergistically with the combined saponin/lipopolysaccharide in the induction of **antigen** specific immune responses leading to enhanced tumor regression. The formulations are potent in the induction of immune responses conventionally associated with Th-1 type immune system. Her 2 neu antigens that are formulated with 3D-MPL, QS21 and **CpG** oligonucleotide together with liposome or oil-in-water emulsion carrier, produce both a humoral and cell mediated response in comparison to the formulations containing only **CpG** that do not produce a significant cell-mediated immune response.

Dwg.0/14

L25 ANSWER 19 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-527359 [56] WPIDS
DNC C2002-149289
TI Method for modulating the **immunostimulatory** effect of an **immunostimulatory oligonucleotide** compound, and new **immunostimulatory oligonucleotide** compounds.
DC B02 D16
IN AGRAWAL, S; KANDIMALLA, E R; YU, D; ZHAO, Q
PA (HYBR-N) HYBRIDON INC; (AGRA-I) AGRAWAL S; (KAND-I) KANDIMALLA E R; (YUDD-I) YU D; (ZHAO-I) ZHAO Q
CYC 96
PI WO 2002026757 A2 20020404 (200256)* EN 94p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001094750 A 20020408 (200256)
US 2002137714 A1 20020926 (200265)
EP 1322656 A2 20030702 (200344) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
ADT WO 2002026757 A2 WO 2001-US30137 20010926; AU 2001094750 A AU 2001-94750
20010926; US 2002137714 A1 Provisional US 2000-235452P 20000926,
Provisional US 2000-235453P 20000926, CIP of US 2000-712898 20001115, US
2001-965116 20010926; EP 1322656 A2 EP 2001-975423 20010926, WO
2001-US30137 20010926
FDT AU 2001094750 A Based on WO 200226757; EP 1322656 A2 Based on WO 200226757
PRAI US 2000-712898 20001115; US 2000-235452P 20000926; US 2000-235453P
20000926; US 2001-965116 20010926
AB WO 200226757 A UPAB: 20020903
NOVELTY - Positional chemical modifications introduced in **immunostimulatory oligonucleotide** compounds affect their **immunostimulatory** capabilities. New **immunostimulatory oligonucleotide** compounds are claimed.
DETAILED DESCRIPTION - A method for modulating the **immunostimulatory** effect of an **immunostimulatory oligonucleotide** compound comprises:
(a) introducing into the immunostimulatory domain a dinucleotide analog that includes a non-naturally occurring pyrimidine base;

(b) introducing into the immunostimulatory domain and/or potentiation domain an immunostimulatory moiety; or

(c) introducing into the oligonucleotide a 3'-3' linkage.

INDEPENDENT CLAIMS are included for the following:

(1) new **immunostimulatory oligonucleotide** compounds comprising:

(a) an immunostimulatory dinucleotide of formula 5'-pyrimidine purine-3', where pyrimidine is a non-natural pyrimidine nucleoside and purine is a natural or non-natural purine nucleoside;

(b) an immunostimulatory dinucleotide of formula C asterisk pG;

(c) immunostimulatory domains of formula 5'-----X1-X2-Y-Z X3-X4-----3' (II);

(d) a sequence of formula 5'-Um..U1-X1-X2-Y-Z-X3-X4D1..m 3' (III) and

(2) a method of generating an immune response comprising administering an oligonucleotide analog described in (1).

C asterisk = a cytidine analog;

G = guanosine, 2'-deoxyguanosine or a guanosine analog;

p = an internucleotide linkage selected from phosphodiester, phosphorothioate and phosphorodithioate;

Y = cytidine, 2'-deoxycytidine, or a non-natural pyrimidine nucleoside;

Z = guanosine, 2'-deoxyguanosine, or a non-natural purine nucleoside;

X1 = a naturally occurring nucleoside or an immunostimulatory moiety selected from a 3C alkyl linker, 2 aminobutyl-1,3-propanediol linker, and beta -L-deoxynucleoside;

X2 = a naturally occurring nucleoside or an immunostimulatory moiety that is an amino linker;

X3 = a naturally occurring nucleoside or an immunostimulatory moiety that is a nucleoside methylphosphonate;

X4 = a naturally occurring nucleoside or an immunostimulatory moiety selected from nucleoside methylphosphonate and 2'-O-methylribonucleoside;

Y = a non-natural pyrimidine nucleoside;

Z = guanosine, 2' deoxy-guanosine or a non-natural purine nucleoside;

X = a naturally occurring nucleoside or an immunostimulatory moiety;

Um-U1 = an upstream potentiation domain where each U is a naturally occurring nucleoside or an immunostimulatory moiety;

D1-Dm = a downstream potentiation domain where each D is a naturally occurring nucleoside or an immunostimulatory moiety; and

m = 0-30.

With the proviso that at least 1 of X1-X4 is an immunostimulatory moiety.

ACTIVITY - Immunostimulatory; Antiviral; Antibacterial; Antiparasitic; Cytostatic; Anti-allergic; Antiasthmatic; Respiratory.

The immunostimulatory activity of end-blocked CpG-PS-oligos was studied in a lymphocyte proliferation assay. Mouse spleen lymphocytes were cultured with CpG-PS-oligos at 0.1, 1 and 10 micro g/ml for 48 hours and cell proliferation was determined by 3H uridine incorporation.

Oligo A induced a dose-dependent effect on cell proliferation (proliferation index (PI) 5.0 plus or minus 0.32 at 10 micro g/ml). Oligo B, which consisted of 2 units of A linked by a 3'-5'-linkage, had PI 5.8 plus or minus 0.28 at the same dose. Oligo C, which consisted of 2 units of A linked by a 5'-5'-linkage, had PI 2.0 plus or minus 0.26, showing a significantly lower immunostimulatory activity than observed for A or B. Oligo D, which consisted of 2 units of A linked by a 3'-3' linkage, had PI 7.2 plus or minus 0.5, showing a greater immunostimulatory activity than observed for A or B.

MECHANISM OF ACTION - None given in the source material.

USE - For treating a disease caused by a pathogen, e.g. a virus, parasite or bacterium; cancer; autoimmune disorders (e.g. autoimmune asthma); or airway inflammation or allergy.

The oligonucleotide may be administered in combination with an

antibiotic, antigen, allergen, vaccine, antibody, cytotoxic agent, antisense oligonucleotide, gene therapy vector, DNA vaccine or adjuvant, particularly with a chemotherapeutic compound in the treatment of cancer.
Dwg.0/28

L25 ANSWER 20 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-362308 [39] WPIDS
CR 2002-351845 [38]
DNC C2002-102545
TI Novel immunogenic composition comprising Streptococcus pneumoniae polysaccharide and protein **antigen** useful for preventing, ameliorating and treating pneumococcal infections in infants, toddlers and elderly persons.
DC B04 D16
IN LAFERRIERE, C A J; POOLMAN, J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS
SA
CYC 98
PI WO 2002022167 A2 20020321 (200239)* EN 42p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2002020548 A 20020326 (200251)
EP 1317279 A2 20030611 (200339) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
BR 2001013821 A 20030624 (200343)
ADT WO 2002022167 A2 WO 2001-EP10568 20010912; AU 2002020548 A AU 2002-20548
20010912; EP 1317279 A2 EP 2001-984626 20010912, WO 2001-EP10568 20010912;
BR 2001013821 A BR 2001-13821 20010912, WO 2001-EP10568 20010912
FDT AU 2002020548 A Based on WO 200222167; EP 1317279 A2 Based on WO
200222167; BR 2001013821 A Based on WO 200222167
PRAI GB 2000-22742 20000915
AB WO 200222167 A UPAB: 20030707
NOVELTY - An immunogenic composition (I) comprising at least one Streptococcus pneumoniae polysaccharide **antigen** and at least one S. pneumoniae protein **antigen** selected from PhtA, PhtD, PhtB, PhtE, SpsA, LytB, LytC, LytA, Sp125, Sp101, Sp128, Sp130 and Sp133, or its immunologically functional equivalent, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a vaccine (II) comprising (I); and
(2) making (I) involves selecting one or more pneumococcal polysaccharide **antigen**(s) and one or more pneumococcal protein **antigen**(s), and mixing the polysaccharide and protein antigens with a suitable excipient.
ACTIVITY - Auditory; antiinflammatory.
No biological data is given.
MECHANISM OF ACTION - Vaccine (claimed); inducer of T-cell mediated response against pneumococcal disease.
The impact of the addition of a Streptococcus pneumoniae protein plus or minus 3D-MPL adjuvant on the protective effectiveness of protein D (PD)-conjugated 11-valent polysaccharide vaccine against pneumococcal lung colonization in OF1 mice intranasally challenged with serotype 2, 4 or 6B was tested. The prophylactic efficacy of a vaccine containing the 11-valent polysaccharide-protein D conjugate, a S. pneumoniae protein and ALPO4+3D-MPL adjuvants, was compared to the classical ALPO4 adsorbed 11-valent polysaccharide-protein D conjugate formulation. Groups of 12 female 4 week old OF1 mice were immunized subcutaneously, with formulations containing 50 mu g ALPO4, 0.1 mg PS/serotype of PD-conjugated

11-valent polysaccharide vaccine + 50 mu g AlPO₄, or 0.1 mu g PS/serotype of PD-conjugated 11-valent polysaccharide vaccine + 10 mu g *S. pneumoniae* protein + 50 mu g AlPO₄ + 5 mu g 3D-MPL. Challenge was done at day 21 as a significant protection was conferred by the 11-valent polysaccharide conjugate vaccine supplemented with the *S. pneumoniae* protein and adjuvanted with AlPO₄+MPL. On the contrary, no significant protection was observed in animals immunized with the 11-valent polysaccharide conjugate/AlPO₄ formulation. This result proved that the addition of the protein and 3D-MPL adjuvant enhanced the effectiveness of the 11-valent polysaccharide conjugate vaccine against pneumonia.

USE - (I) is useful as a medicament. (II) is useful for preventing or ameliorating *S. pneumoniae* infection in a patient over 55 years, or in the manufacture of a medicament for the prevention or treatment of pneumonia in a patient over 55 years. (I) or (II) is useful in the manufacture of a medicament for preventing, ameliorating or treating otitis media in infants or toddlers (claimed).

Dwg.0/0

=> d bib 21-82

L25 ANSWER 21 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2002:122818 CAPLUS
 DN 136:182447
 TI Vaccine against respiratory syncytial virus (RSV)
 IN Mond, James J.; Prince, Gregory; Klinman, Dennis M.
 PA Henry M. Jackson Foundation for the Advancement of Military Medicine, USA
 SO PCT Int. Appl., 30 pp.
 CODEN: PIXXD2

DT Patent
 LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002011761	A2	20020214	WO 2001-US41633	20010809
	WO 2002011761	A3	20030123		
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	AU 2001085421	A5	20020218	AU 2001-85421	20010809
PRAI	US 2000-224011P	P	20000810		
	US 2000-229307P	P	20000901		
	WO 2001-US41633	W	20010809		

L25 ANSWER 22 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2002:736889 CAPLUS
 DN 137:273194
 TI Modulation of **immunostimulatory** activity of **immunostimulatory oligonucleotide** analogs by positional chemical changes
 IN Kandimalla, Ekambar R.; Zhao, Qiuyan; Yu, Dong; Agrawal, Sudhir
 PA USA
 SO U.S. Pat. Appl. Publ., 41 pp., Cont.-in-part of U.S. Ser. No. 712,898.
 CODEN: USXXCO

DT Patent
 LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002137714	A1	20020926	US 2001-965116	20010926
PRAI	US 2000-235452P	P	20000926		
	US 2000-235453P	P	20000926		
	US 2000-712898	A2	20001115		

OS MARPAT 137:273194

L25 ANSWER 23 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:588977 CAPLUS

DN 137:135079

TI Immunostimulatory nucleic acid molecules for activating dendritic cells, and therapeutic use

IN Krieg, Arthur M.; Hartmann, Gunther

PA University of Iowa Research Foundation, USA

SO U.S., 52 pp., Cont.-in-part of U.S. 6,239,116.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6429199	B1	20020806	US 1998-191170	19981113
	US 6008200	A	19991228	US 1995-386063	19950207
	US 6194388	B1	20010227		
	EP 1167377	A2	20020102	EP 2001-202811	19950207
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	EP 1167378	A2	20020102	EP 2001-202813	19950207
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	EP 1167379	A2	20020102	EP 2001-202814	19950207
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 2003144184	A2	20030520	JP 2002-302338	19950207
	US 6207646	B1	20010327	US 1996-738652	19961030
	US 6239116	B1	20010529	US 1997-960774	19971030
	US 2003100527	A1	20030529	US 2002-161229	20020603
PRAI	US 1994-276358	B2	19940715		
	US 1995-386063	A2	19950207		
	US 1996-738652	A2	19961030		
	US 1997-960774	A2	19971030		
	EP 1995-911630	A3	19950207		
	JP 1996-504991	A3	19950207		
	US 1998-191170	A3	19981113		

OS MARPAT 137:135079

RE.CNT 177 THERE ARE 177 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 24 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:461200 CAPLUS

DN 137:32060

TI Use of nucleic acids containing unmethylated CpG dinucleotide as an adjuvant

IN Davis, Heather L.; Schorr, Joachim; Krieg, Arthur M.

PA University of Iowa Research Foundation, USA

SO U.S., 53 pp., Cont.-in-part of U.S. Ser. No. 154,614.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6406705	B1	20020618	US 1999-325193	19990603
	WO 9840100	A1	19980917	WO 1998-US4703	19980310
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,				

DT Conference
LA English

L25 ANSWER 32 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 13
AN 2002:484833 BIOSIS
DN PREV200200484833
TI Reversal of tumor-induced dendritic cell paralysis by **CpG immunostimulatory oligonucleotide** and anti-interleukin 10 receptor antibody.
AU Vicari, Alain P. (1); Chiodoni, Claudia; Vaure, Celine; Ait-Yahia, Smina; Dercamp, Christophe; Matsos, Fabien; Reynard, Olivier; Taverne, Catherine; Merle, Philippe; Colombo, Mario P.; O'Garra, Anne; Trinchieri, Giorgio; Caux, Christophe
CS (1) Schering-Plough Laboratory for Immunological Research, 27 Chemin des Peupliers, 69571, BP11, Dardilly: alain.vicari@spcorp.com France
SO Journal of Experimental Medicine, (August 19, 2002) Vol. 196, No. 4, pp. 541-549. <http://www.jem.org>. print.
ISSN: 0022-1007.
DT Article
LA English

L25 ANSWER 33 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:353888 BIOSIS
DN PREV200200353888
TI Effective immunotherapy of large established tumors with **CpG** oligonucleotides and dendritic cells in murine tumor models.
AU Hartmann, Gunther (1); Heckelsmiller, Klaus (1); Rall, Katharina (1); Endres, Stefan (1)
CS (1) Department of Internal Medicine, Division of Clinical Pharmacology, University of Munich, Ziemssenstrasse 1, Munich, Bavaria, 80336 Germany
SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A334. <http://www.fasebj.org/>. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DT Conference
LA English

L25 ANSWER 34 OF 82 WPIDS. COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 14
AN 2002-130570 [17] WPIDS
DNC C2002-040090
TI New **immunostimulatory** compositions comprising RNA/DNA hybrid **oligonucleotides**, useful for enhancing an immune response or inducing cytokines, particularly for treating diseases, e.g. cancer, allergy or HIV infection.
DC B04 D16
IN FLORA, M; KLINMAN, D M; MOND, J J
PA (BIOS-N) BIOSYNEXUS INC
CYC 96
PI WO 2001093902 A2 20011213 (200217)* EN 68p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001075294 A 20011217 (200225)
EP 1292331 A2 20030319 (200322) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
ADT WO 2001093902 A2 WO 2001-US18276 20010607; AU 2001075294 A AU 2001-75294
20010607; EP 1292331 A2 EP 2001-941989 20010607, WO 2001-US18276 20010607

FDT AU 2001075294 A Based on WO 200193902; EP 1292331 A2 Based on WO 200193902
PRAI US 2000-209797P 20000607

L25 ANSWER 35 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 15
AN 2001-122974 [13] WPIDS
CR 2001-476172 [51]
DNC C2001-035668

TI New vaccine formulation comprising human immunodeficiency virus (HIV)
antigen and **immunostimulatory CpG**
oligonucleotide, useful for preventing and treating HIV infections
in a patient.

DC B04 D16

IN GARCON, N; VOSS, G

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (SMIK) SMITHKLINE BEECHAM BIOLOGICS
SA

CYC 95

PI WO 2001000232 A2 20010104 (200113)* EN 23p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000058210 A 20010131 (200124)

AU 2001057910 A 20010807 (200174)

EP 1198249 A2 20020424 (200235) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL RO
SI

SK 2002001112 A3 20030109 (200309)

KR 2002073569 A 20020927 (200311)

CZ 2002002643 A3 20030212 (200317)

ADT WO 2001000232 A2 WO 2000-EP5998 20000628; AU 2000058210 A AU 2000-58210
20000628; AU 2001057910 A AU 2001-57910 20010129; EP 1198249 A2 EP
2000-943919 20000628, WO 2000-EP5998 20000628; SK 2002001112 A3 WO
2001-EP944 20010129, SK 2002-1112 20010129; KR 2002073569 A KR 2002-709825
20020730; CZ 2002002643 A3 WO 2001-EP944 20010129, CZ 2002-2643 20010129

FDT AU 2000058210 A Based on WO 200100232; AU 2001057910 A Based on WO
200154719; EP 1198249 A2 Based on WO 200100232; SK 2002001112 A3 Based on
WO 200154719; CZ 2002002643 A3 Based on WO 200154719

PRAI GB 2000-2200 20000131; GB 1999-15205 19990629; GB 2000-9336
20000414; GB 2000-13806 20000606

L25 ANSWER 36 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 16
AN 2001-112392 [12] WPIDS
DNC C2001-033426

TI New vaccine formulation, useful for preventing and treating plasmodium
infection in a patient, comprises malaria **antigen** and
immunostimulatory CpG oligonucleotide.

DC B04 D16

IN COHEN, J; GARCON, N; VOSS, G

PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS

CYC 95

PI WO 2001000231 A2 20010104 (200112)* EN 21p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000059777 A 20010131 (200124)

EP 1198243 A2 20020424 (200235) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

ADT WO 2001000231 A2 WO 2000-EP5841 20000623; AU 2000059777 A AU 2000-59777
20000623; EP 1198243 A2 EP 2000-945810 20000623, WO 2000-EP5841 20000623
FDT AU 2000059777 A Based on WO 200100231; EP 1198243 A2 Based on WO 200100231
PRAI GB 1999-15204 19990629

L25 ANSWER 37 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 17
AN 2001-217934 [22] WPIDS
CR 1996-105847 [11]; 1998-272127 [24]; 2000-086224 [07]; 2001-280761 [29];
2001-380456 [40]; 2002-689667 [74]; 2003-466135 [44]; 2003-512356 [48]
DNC C2001-064962
TI Immunostimulatory composition useful for stimulating immune response in a
subject, comprises **antigen** and **immunostimulatory**
nucleic acid comprising **oligonucleotides** having unmethylated
cytosine-guanine dinucleotides.
DC B04 D16
IN KLINMAN, D; KRIEG, A M; STEINBERG, A D
PA (COLE-N) COLEY PHARM GROUP; (IOWA) UNIV IOWA RES FOUND
CYC 1
PI US 6194388 B1 20010227 (200122)* 20p
ADT US 6194388 B1 CIP of US 1994-276358 19940715, US 1995-386063 19950207
PRAI US 1995-386063 19950207; US 1994-276358 19940715

L25 ANSWER 38 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:935435 CAPLUS
DN 136:84677
TI Methods for enhancing antibody-induced cell lysis and treating cancer
IN Weiner, George; Hartmann, Gunther
PA University of Iowa Research Foundation, USA
SO PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001097843	A2	20011227	WO 2001-US20154	20010622
	WO 2001097843	A3	20030123		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2003026801	A1	20030206	US 2001-888326	20010622
	EP 1296714	A2	20030402	EP 2001-948684	20010622
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	US 2000-213346P	P	20000622		
	WO 2001-US20154	W	20010622		

L25 ANSWER 39 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:816708 CAPLUS
DN 135:356755
TI Nucleic acid immunization
IN Haynes, Joel R.; Macklin, Michael D.; Payne, Lendon G.
PA Powderject Vaccines, Inc., USA; Powderject Research Limited
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001083528	A2	20011108	WO 2001-GB1924	20010501
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002165176	A1	20021107	US 2001-846091	20010430
	EP 1282640	A2	20030212	EP 2001-925706	20010501
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-200968P	P	20000501		
	US 2000-561951	A	20000501		
	US 2000-210580P	P	20000608		
	WO 2001-GB1924	W	20010501		

L25 ANSWER 40 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2001:247187 CAPLUS

DN 134:275762

TI Immunostimulatory nucleic acids

IN Krieg, Arthur M.; Schetter, Christian; Vollmer, Jorg

PA University of Iowa Research Foundation, USA; Coley Pharmaceutical G.b.m.H.

SO PCT Int. Appl., 338 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001022972	A2	20010405	WO 2000-US26383	20000925
	WO 2001022972	A3	20020117		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1221955	A2	20020717	EP 2000-965433	20000925
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	BR 2000014236	A	20021015	BR 2000-14236	20000925
	JP 2003510282	T2	20030318	JP 2001-526182	20000925
	EE 200200158	A	20030616	EE 2002-158	20000925
	BG 106538	A	20021229	BG 2002-106538	20020321
	NO 2002001453	A	20020527	NO 2002-1453	20020322
PRAI	US 1999-156113P	P	19990925		
	US 1999-156135P	P	19990927		
	US 2000-227436P	P	20000823		
	WO 2000-US26383	W	20000925		
OS	MARPAT 134:275762				

L25 ANSWER 41 OF 82 MEDLINE on STN

DUPLICATE 18

AN 2001495673 MEDLINE

DN 21429315 PubMed ID: 11544321

L25 ANSWER 48 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:565972 BIOSIS
 DN PREV200200565972
 TI **Immunostimulatory oligonucleotide** (ISS ODN)
 co-injection enhances protective antibody response to Hepatitis B surface
antigen (HBsAg) and is well-tolerated by seronegative individuals.
 AU Halperin, S. A. (1); Van Nest, G.; Halperin, B. (1); Smith, B. (1);
 Abtahi, S.; Whiley, H.; Eiden, J.
 CS (1) Dalhousie Univ., Halifax, NS Canada
 SO Abstracts of the Interscience Conference on Antimicrobial Agents and
 Chemotherapy, (2001) Vol. 41, pp. 276. print.
 Meeting Info.: 41st Annual Meeting of the Interscience Conference on
 Antimicrobial Agents and Chemotherapy Chicago, Illinois, USA September
 22-25, 2001
 DT Article
 LA English

L25 ANSWER 49 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:153098 BIOSIS
 DN PREV200200153098
 TI The level of cell surface expression of TLR-9 does not correlate with the
 degree of activation mediated by immunostimulatory DNA sequences in
 patients with B cell CLL.
 AU Castro, Januario E. (1); Motta, Marina; Kipps, Thomas J. (1)
 CS (1) Department of Medicine, Division of Hematology-Oncology, UCSD, San
 Diego, CA USA
 SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 152a.
<http://www.bloodjournal.org/>. print.
 Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
 Part 1 Orlando, Florida, USA December 07-11, 2001
 ISSN: 0006-4971.
 DT Conference
 LA English

L25 ANSWER 50 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 19
 AN 2002:97794 BIOSIS
 DN PREV200200097794
 TI **CpG** ODN can re-direct the Th bias of established Th2 immune
 responses in adult and young mice.
 AU Weeratna, Risini D. (1); Brazolot Millan, Cynthia L.; McCluskie, Michael
 J.; Davis, Heather L.
 CS (1) Coley Pharmaceutical Canada, 725 Parkdale Avenue, Ottawa, ON, K1Y 4E9:
 rweeratna@coleypharma.com Canada
 SO FEMS Immunology and Medical Microbiology, (December, 2001) Vol. 32, No. 1,
 pp. 65-71. print.
 ISSN: 0928-8244.
 DT Article
 LA English

L25 ANSWER 51 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 20
 AN 2001:332939 BIOSIS
 DN PREV200100332939
 TI Enhancement of **antigen**-presenting ability of B lymphoma cells by
immunostimulatory CpG-oligonucleotides and
 anti-CD40 antibody.
 AU Chen, Weilin; Yu, Yizhi; Shao, Chuansen; Zhang, Minhui; Wang, Wenya;
 Zhang, Lihuang; Cao, Xuetao (1)
 CS (1) Institute of Immunology, Zhejiang University, Hangzhou, Zhejiang,
 310031: caoxt@public3.sta.net.cn China
 SO Immunology Letters, (May 1, 2001) Vol. 77, No. 1, pp. 17-23. print.
 ISSN: 0165-2478.

DT Article
LA English
SL English

L25 ANSWER 52 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:197665 CAPLUS
TI Structure-activity relationships of **immunostimulatory oligonucleotides**
AU Kandimalla, E. R.; Zhao, Q.; Yu, D.; Agrawal, S.
CS Hybridon, Inc, Cambridge, MA, 02139, USA
SO Abstracts of Papers - American Chemical Society (2001), 221st, CARB-012
CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English

L25 ANSWER 53 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 21
AN 2000-679550 [66] WPIDS
CR 2000-594515 [55]; 2000-594516 [55]; 2000-594517 [55]; 2001-006956 [61]
DNC C2000-206694
TI Novel vaccine formulation comprising a respiratory syncytial virus (RSV) **antigen** and an **immunostimulatory CpG oligonucleotide** useful for treating RSV infections mutations.
DC B04 D16
IN DESCHAMPS, M
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 92
PI WO 2000062802 A2 20001026 (200066)* EN 34p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE
ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000045525 A 20001102 (200107)
EP 1171158 A2 20020116 (200207) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
ADT WO 2000062802 A2 WO 2000-EP3516 20000417; AU 2000045525 A AU 2000-45525
20000417; EP 1171158 A2 EP 2000-926986 20000417, WO 2000-EP3516 20000417
FDT AU 2000045525 A Based on WO 200062802; EP 1171158 A2 Based on WO 200062802
PRAI GB 1999-15106 19990628; GB 1999-9077 19990420

L25 ANSWER 54 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 22
AN 2000-594516 [56] WPIDS
CR 2000-594515 [56]; 2000-594517 [56]; 2000-679550 [66]; 2001-006956 [01]
DNC C2000-177616
TI Novel immunogenic composition comprising at least 1 polysaccharide **antigen** and at least 1 protein **antigen** from *Streptococcus pneumoniae*, useful in vaccines for treating pneumonia and otitis media.
DC B04 D16
IN CAPIAU, C; DESCHAMPS, M; DESMONS, P M; LAFERRIERE, C A J; POOLMAN, J;
PRIELS, J; FERRIERE, C A J
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 92
PI WO 2000056359 A2 20000928 (200056)* EN 77p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE
ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000038136 A 20001009 (200103)
 BR 2000009166 A 20011226 (200206)
 EP 1162999 A2 20011219 (200206) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 CZ 2001003379 A3 20020313 (200223)
 KR 2002001785 A 20020109 (200246)
 HU 2002000373 B 20020628 (200255)
 AU 750762 B 20020725 (200260)
 ZA 2001007638 A 20020828 (200264) 97p
 JP 2002540074 W 20021126 (200307) 97p
 CN 1391481 A 20030115 (200330)
 ADT WO 2000056359 A2 WO 2000-EP2467 20000317; AU 2000038136 A AU 2000-38136
 20000317; BR 2000009166 A BR 2000-9166 20000317, WO 2000-EP2467 20000317;
 EP 1162999 A2 EP 2000-916983 20000317, WO 2000-EP2467 20000317; CZ
 2001003379 A3 WO 2000-EP2467 20000317, CZ 2001-3379 20000317; KR
 2002001785 A WO 2000-EP2467 20000317, KR 2001-711941 20010919; HU
 2002000373 B WO 2000-EP2467 20000317, HU 2002-373 20000317; AU 750762 B AU
 2000-38136 20000317; ZA 2001007638 A ZA 2001-7638 20010917; JP 2002540074
 W JP 2000-606263 20000317, WO 2000-EP2467 20000317; CN 1391481 A CN
 2000-807773 20000317
 FDT AU 2000038136 A Based on WO 200056359; BR 2000009166 A Based on WO
 200056359; EP 1162999 A2 Based on WO 200056359; CZ 2001003379 A3 Based on
 WO 200056359; KR 2002001785 A Based on WO 200056359; HU 2002000373 B Based
 on WO 200056359; AU 750762 B Previous Publ. AU 200038136, Based on WO
 200056359; JP 2002540074 W Based on WO 200056359
 PRAI GB 1999-16677 19990715; GB 1999-6437 19990319; GB 1999-9077
 19990420; GB 1999-9466 19990423
 L25 ANSWER 55 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 23
 AN 2000-224181 [19] WPIDS
 CR 2001-451816 [48]
 DNC C2000-068362
 TI A vaccine composition comprising an **antigen**, saponin adjuvant
 and **immunostimulatory CpG oligonucleotide**,
 useful for stimulating immunity and increasing immune responses.
 DC B04 D16
 IN KENSIL, C A; KENSIL, C
 PA (AQUI-N) AQUILA BIOPHARMACEUTICALS INC; (KENS-I) KENSIL C
 CYC 88
 PI WO 2000009159 A1 20000224 (200019)* EN 38p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK EE ES FI
 GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
 LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT UA UG US UZ VN YU ZA ZW
 AU 9953953 A 20000306 (200030)
 EP 1104306 A1 20010606 (200133) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 US 2001034330 A1 20011025 (200170)
 JP 2002522510 W 20020723 (200263) 41p
 ADT WO 2000009159 A1 WO 1999-US17956 19990806; AU 9953953 A AU 1999-53953
 19990806; EP 1104306 A1 EP 1999-939711 19990806, WO 1999-US17956 19990806;
 US 2001034330 A1 Provisional US 1998-95913P 19980810, Provisional US
 1999-128608P 19990408, Provisional US 2000-175840P 20000113, Provisional
 US 2000-200853P 20000501, US 2001-760506 20010112; JP 2002522510 W WO
 1999-US17956 19990806, JP 2000-564661 19990806
 FDT AU 9953953 A Based on WO 200009159; EP 1104306 A1 Based on WO 200009159;
 JP 2002522510 W Based on WO 200009159
 PRAI US 1999-128608P 19990408; US 1998-95913P 19980810; US 2000-175840P
 20000113; US 2000-200853P 20000501; US 2001-760506 20010112

L25 ANSWER 56 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 24
AN 2000-195254 [17] WPIDS
DNC C2000-060544
TI **Immunostimulatory** and immunoinhibitory stereoisomers of
CpG oligonucleotides useful for immunotherapy of cancer.
DC B04 D16
IN KRIEG, A M
PA (CPGI-N) CPG IMMUNOPHARMACEUTICALS INC; (IOWA) UNIV IOWA RES FOUND
CYC 86
PI WO 2000006588 A1 20000210 (200017)* EN 88p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG UZ VN YU ZA ZW
AU 9953238 A 20000221 (200029)
EP 1100807 A1 20010523 (200130) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
JP 2002521489 W 20020716 (200261) 104p
ADT WO 2000006588 A1 WO 1999-US17100 19990727; AU 9953238 A AU 1999-53238
19990727; EP 1100807 A1 EP 1999-938843 19990727, WO 1999-US17100 19990727;
JP 2002521489 W WO 1999-US17100 19990727, JP 2000-562385 19990727
FDT AU 9953238 A Based on WO 200006588; EP 1100807 A1 Based on WO 200006588;
JP 2002521489 W Based on WO 200006588
PRAI US 1998-94370P 19980727

L25 ANSWER 57 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 25
AN 2000-566166 [53] WPIDS
DNC C2000-168850
TI Pharmaceutical composition useful for tumor therapy comprises
tumor-reactive helper T cells that produce high levels of interferon gamma
and little or no interleukin-4.
DC B04 D16
IN EGETER, O; MOCIKAT, R; ROECKEN, M; ROCKEN, M
PA (EGET-I) EGETER O; (GSFU-N) GSF FORSCHUNGSZENTRUM UMWELT & GESUNDHEI;
(ROEC-I) ROECKEN M; (MOCI-I) MOCIKAT R; (ROCK-I) ROCKEN M
CYC 22
PI DE 19906744 A1 20000824 (200053)* 9p
WO 2000048614 A2 20000824 (200053) DE
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 1152767 A2 20011114 (200175) DE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2002068053 A1 20020606 (200241)#
JP 2002537265 W 20021105 (200304) 34p
ADT DE 19906744 A1 DE 1999-19906744 19990218; WO 2000048614 A2 WO 2000-EP1339
20000217; EP 1152767 A2 EP 2000-912481 20000217, WO 2000-EP1339 20000217;
US 2002068053 A1 Cont of WO 2000-EP1339 20000217, US 2001-932575 20010816;
JP 2002537265 W JP 2000-599404 20000217, WO 2000-EP1339 20000217
FDT EP 1152767 A2 Based on WO 2000048614; JP 2002537265 W Based on WO 2000048614
PRAI DE 1999-19906744 19990218; US 2001-932575 20010816

L25 ANSWER 58 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-687101 [67] WPIDS
CR 2002-471376 [50]
DNC C2000-209017
TI Adjuvant composition comprising saponin and **immunostimulatory**
oligonucleotide CpG, useful for producing vaccine
formulations for prophylaxis and treatment of cancers, allergy and
Alzheimer's disease.

DC B04 D16
 IN FRIEDE, M; GARCON, N; HERMAND, P; GERARD, C M G
 PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
 CYC 92
 PI WO 2000062800 A2 20001026 (200067)* EN 52p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE
 ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
 LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK
 SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000041149 A 20001102 (200107)
 NO 2001005073 A 20011122 (200211)
 BR 2000010612 A 20020213 (200220)
 CZ 2001003774 A3 20020313 (200223)
 EP 1187629 A2 20020320 (200227) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 HU 2002000815 A2 20020828 (200264)
 JP 2002542203 W 20021210 (200301) 65p
 ZA 2001008619 A 20021127 (200305) 70p
 CN 1372473 A 20021002 (200307)
 KR 2002067617 A 20020823 (200310)
 US 6544518 B1 20030408 (200327)
 ADT WO 2000062800 A2 WO 2000-EP2920 20000404; AU 2000041149 A AU 2000-41149
 20000404; NO 2001005073 A WO 2000-EP2920 20000404, NO 2001-5073 20011018;
 BR 2000010612 A BR 2000-10612 20000404, WO 2000-EP2920 20000404; CZ
 2001003774 A3 WO 2000-EP2920 20000404, CZ 2001-3774 20000404; EP 1187629
 A2 EP 2000-920647 20000404, WO 2000-EP2920 20000404; HU 2002000815 A2 WO
 2000-EP2920 20000404, HU 2002-815 20000404; JP 2002542203 W JP 2000-611936
 20000404, WO 2000-EP2920 20000404; ZA 2001008619 A ZA 2001-8619 20011019;
 CN 1372473 A CN 2000-808836 20000404; KR 2002067617 A KR 2001-713357
 20011019; US 6544518 B1 CIP of US 1999-301829 19990429, CIP of WO
 2000-EP2920 20000404, US 2000-690921 20001018
 FDT AU 2000041149 A Based on WO 200062800; BR 2000010612 A Based on WO
 200062800; CZ 2001003774 A3 Based on WO 200062800; EP 1187629 A2 Based on
 WO 200062800; HU 2002000815 A2 Based on WO 200062800; JP 2002542203 W
 Based on WO 200062800
 PRAI US 1999-301829 19990429; GB 1999-8885 19990419
 L25 ANSWER 59 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 2000-594517 [56] WPIDS
 CR 2000-594515 [56]; 2000-594516 [56]; 2000-679550 [66]; 2001-006956 [01]
 DNC C2000-177617
 TI A Streptococcus pneumoniae vaccine for preventing pneumonia and meningitis
 comprises a polysaccharide **antigen** conjugated to protein D from
 Haemophilus influenzae.
 DC B04 D16
 IN CAPIAU, C; DESCHAMPS, M; DESMONS, P M; LAFERRIERE, C A J; POOLMAN, J;
 PRIEELS, J; POOLMAN, J P J
 PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
 CYC 93
 PI WO 2000056360 A2 20000928 (200056)* EN 77p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000034307 A 20001009 (200103)
 BR 2000009163 A 20011226 (200206)
 EP 1163000 A2 20011219 (200206) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI

CZ 2001003380 A3 20020313 (200223)
 KR 2002000549 A 20020105 (200244)
 HU 2002000367 B 20020528 (200249)
 CN 1351503 A 20020529 (200258)
 AU 750913 B 20020801 (200261)
 ZA 2001007637 A 20020828 (200264) 97p
 JP 2002540075 W 20021126 (200307) 96p

ADT WO 2000056360 A2 WO 2000-EP2468 20000317; AU 2000034307 A AU 2000-34307
 20000317; BR 2000009163 A BR 2000-9163 20000317, WO 2000-EP2468 20000317;
 EP 1163000 A2 EP 2000-912626 20000317, WO 2000-EP2468 20000317; CZ
 2001003380 A3 WO 2000-EP2468 20000317, CZ 2001-3380 20000317; KR
 2002000549 A WO 2000-EP2468 20000317, KR 2001-711939 20010919; HU
 2002000367 B WO 2000-EP2468 20000317, HU 2002-367 20000317; CN 1351503 A
 CN 2000-807528 20000317; AU 750913 B AU 2000-34307 20000317; ZA 2001007637
 A ZA 2001-7637 20010917; JP 2002540075 W JP 2000-606264 20000317, WO
 2000-EP2468 20000317

FDT AU 2000034307 A Based on WO 200056360; BR 2000009163 A Based on WO
 200056360; EP 1163000 A2 Based on WO 200056360; CZ 2001003380 A3 Based on
 WO 200056360; KR 2002000549 A Based on WO 200056360; HU 2002000367 B Based
 on WO 200056360; AU 750913 B Previous Publ. AU 200034307, Based on WO
 200056360; JP 2002540075 W Based on WO 200056360

PRAI GB 1999-16677 19990715; GB 1999-6437 19990319; GB 1999-9077
 19990420; GB 1999-9466 19990423

L25 ANSWER 60 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:666624 CAPLUS

DN 133:251267

TI Immunostimulatory nucleic acids and antigens

IN Sosin, Howard B.; Caplan, Michael J.

PA Panacea Pharmaceuticals, LLC, USA

SO PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000054803	A2	20000921	WO 2000-US7213	20000316
	WO 2000054803	A3	20010111		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
 DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
 MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
 TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-124595P P 19990316

US 1999-125071P P 19990317

L25 ANSWER 61 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:708095 CAPLUS

DN 134:4001

TI Effects of a hexameric deoxyriboseguanosine run conjugation into CpG
 oligodeoxynucleotides on their immunostimulatory potentials

AU Lee, Seung Woo; Song, Man Ki; Baek, Kwan Hyuck; Park, Yunji; Kim, Jong
 Kyung; Lee, Chu Hee; Cheong, Hae-Kap; Cheong, Chaejoon; Sung, Young Chul

CS Department of Life Science, Center for Biofunctional Molecules, Pohang
 University of Science and Technology, Pohang, 790-784, S. Korea

SO Journal of Immunology (2000), 165(7), 3631-3639

CODEN: JOIMA3; ISSN: 0022-1767

ISSN: 0019-2805.

DT Article
LA English
SL English

L25 ANSWER 69 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:526175 CAPLUS

DN 134:250881

TI In vivo **antigen** loading and activation of dendritic cells via a liposomal peptide vaccine mediates protective antiviral and anti-tumour immunity

AU Ludewig, B.; Barchiesi, F.; Pericin, M.; Zinkernagel, R. M.; Hengartner, H.; Schwendener, R. A.

CS Department of Pathology, Institute of Experimental Immunology, University of Zurich, Zurich, CH-8091, Switz.

SO Vaccine (2000), 19(1), 23-32

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier Science Ltd.

DT Journal

LA English

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 70 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 2000:113513 BIOSIS

DN PREV2000000113513

TI Immunostimulatory bacterial DNA sequences activate dendritic cells and promote priming and differentiation of CD8+ T cells.

AU Tascon, R. E.; Ragno, S.; Lowrie, D. B.; Colston, M. J. (1)

CS (1) Mycobacterial Division, National Institute for Medical Research, Ridgeway, Mill Hill, London, NW7 1AA UK

SO Immunology, (Jan., 2000) Vol. 99, No. 1, pp. 1-7.

ISSN: 0019-2805.

DT Article

LA English

SL English

L25 ANSWER 71 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 31

AN 1999-620169 [53] WPIDS

DNC C1999-180952

TI Novel synergistic combinations of **immunostimulatory oligonucleotides** and immunopotentiating cytokines are useful for stimulating the immune system.

DC B04 D16

IN KRIEG, A M; WEINER, G

PA (IOWA) UNIV IOWA RES FOUND; (KRIE-I) KRIEG A M; (WEIN-I) WEINER G

CYC 87

PI WO 9951259 A2 19991014 (199953)* EN 91p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG UZ VN YU ZA ZW

AU 9934678 A 19991025 (200011)

EP 1067956 A2 20010117 (200105) EN

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

US 6218371 B1 20010417 (200123)

JP 2002510644 W 20020409 (200227) 119p

US 2002064515 A1 20020530 (200240)

AU 760549 B 20030515 (200337)

ADT WO 9951259 A2 WO 1999-US7335 19990402; AU 9934678 A AU 1999-34678
19990402; EP 1067956 A2 EP 1999-916332 19990402; WO 1999-US7335 19990402;

US 6218371 B1 Provisional US 1998-80729P 19980403, US 1999-286098
19990402; JP 2002510644 W WO 1999-US7335 19990402, JP 2000-542030
19990402; US 2002064515 A1 Provisional US 1998-80729P 19980403, Div ex US
1999-286098 19990402, US 2001-824468 20010402; AU 760549 B AU 1999-34678
19990402

FDT AU 9934678 A Based on WO 9951259; EP 1067956 A2 Based on WO 9951259; JP
2002510644 W Based on WO 9951259; US 2002064515 A1 Div ex US 6218371; AU
760549 B Previous Publ. AU 9934678, Based on WO 9951259

PRAI US 1998-80729P 19980403; US 1999-286098 19990402; US 2001-824468
20010402

L25 ANSWER 72 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 32
AN 1999-405369 [34] WPIDS
CR 1999-405485 [34]
DNC C1999-119689
TI A vaccine composition for inducing a immune response to T-independent type
1 or type 2 **antigen** or polysaccharide conjugate **antigen**

DC B04 D16
IN DALEMANS, W L J; LAFERRIERE, C A J; PRIEELS, J; GERARD, C M; DALEMANS, W;
GERARD, C M G
PA (SMIK) SMITHKLINE BEECHAM BIOLOGICALS
CYC 86
PI WO 9933488 A2 19990708 (199934)* EN 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG US UZ VN YU ZW

AU 9924190 A 19990719 (199951)
ZA 9811849 A 20000726 (200042) 35p
EP 1039930 A2 20001004 (200050) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI
NO 2000003303 A 20000804 (200050)
NO 2000003302 A 20000818 (200052)
BR 9814483 A 20001010 (200055)
CZ 2000002375 A3 20001115 (200064)
CN 1284884 A 20010221 (200131)
CN 1284885 A 20010221 (200131)
AU 736099 B 20010726 (200149)
KR 2001033613 A 20010425 (200164)
KR 2001033618 A 20010425 (200164)
MX 2000006323 A1 20010201 (200168)
MX 2000006324 A1 20010201 (200168)
JP 2001527050 W 20011225 (200204) 42p
HU 2001003085 A2 20011128 (200209)
NZ 505107 A 20030328 (200325)

ADT WO 9933488 A2 WO 1998-EP8562 19981218; AU 9924190 A AU 1999-24190
19981218; ZA 9811849 A ZA 1998-11849 19981223; EP 1039930 A2 EP
1998-966705 19981218, WO 1998-EP8562 19981218; NO 2000003303 A WO
1998-EP8563 19981218, NO 2000-3303 20000623; NO 2000003302 A WO
1998-EP8562 19981218, NO 2000-3302 20000623; BR 9814483 A BR 1998-14483
19981218, WO 1998-EP8562 19981218; CZ 2000002375 A3 WO 1998-EP8562
19981218, CZ 2000-2375 19981218; CN 1284884 A CN 1998-813794 19981218; CN
1284885 A CN 1998-813795 19981218; AU 736099 B AU 1999-24190 19981218; KR
2001033613 A KR 2000-707126 20000624; KR 2001033618 A KR 2000-707131
20000624; MX 2000006323 A1 MX 2000-6323 20000623; MX 2000006324 A1 MX
2000-6324 20000623; JP 2001527050 W WO 1998-EP8562 19981218, JP
2000-526239 19981218; HU 2001003085 A2 WO 1998-EP8562 19981218, HU
2001-3085 19981218; NZ 505107 A NZ 1998-505107 19981218, WO 1998-EP8562
19981218

FDT AU 9924190 A Based on WO 9933488; EP 1039930 A2 Based on WO 9933488; BR

9814483 A Based on WO 9933488; CZ 2000002375 A3 Based on WO 9933488; AU 736099 B Previous Publ. AU 9924190, Based on WO 9933488; JP 2001527050 W Based on WO 9933488; HU 2001003085 A2 Based on WO 9933488; NZ 505107 A Based on WO 9933488

PRAI GB 1997-27262 19971224

L25 ANSWER 73 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-086224 [07] WPIDS
CR 1996-105847 [11]; 1998-272127 [24]; 2001-217934 [22]; 2001-280761 [29]; 2001-380456 [40]; 2002-689667 [74]; 2003-466135 [44]; 2003-512356 [48]
DNC C2000-023992
TI **Immunostimulatory oligonucleotides** which enhance B cell activation useful for treating an immune system deficiency e.g. cancer?
DC B04 D16
IN KRIEG, A M
PA (IOWA) UNIV IOWA RES FOUND
CYC 1
PI US 6008200 A 19991228 (200007)* 19p
ADT US 6008200 A CIP of US 1994-276358 19940715, US 1995-386063 19950207
PRAI US 1995-386063 19950207; US 1994-276358 19940715

L25 ANSWER 74 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:763900 CAPLUS
DN 132:11626
TI **CpG** oligonucleotides and other adjuvants for inducing mucosal immunity
IN McCluskie, Michael J.; Davis, Heather L.
PA Loeb Health Research Institute At the Ottawa Hospital, Can.; CPG Immunopharmaceuticals, Inc.
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961056	A2	19991202	WO 1999-US11359	19990521
	WO 9961056	A3	20000406		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2328894	AA	19991202	CA 1999-2328894	19990521
	AU 9941977	A1	19991213	AU 1999-41977	19990521
	AU 761899	B2	20030612		
	EP 1077722	A2	20010228	EP 1999-925754	19990521
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9910643	A	20011030	BR 1999-10643	19990521
	JP 2002516294	T2	20020604	JP 2000-550515	19990521
PRAI	US 1998-86393P	P	19980522		
	WO 1999-US11359	W	19990521		

L25 ANSWER 75 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:722906 CAPLUS
DN 131:356095
TI Methods for the prevention and treatment of parasitic infections and

AN 1999-080827 [07] WPIDS
 CR 1999-059898 [05]
 DNC C1999-024197
 TI New **oligonucleotide** that inhibits action of
immunostimulatory sequence **oligonucleotides** -
 particularly those present in gene therapy vectors or microbial pathogens,
 used to prolong gene therapy expression and to treat e.g. infections or
 autoimmune disease.
 DC B04 D16
 IN RAY, E; ROMAN, M; RAZ, E
 PA (REGC) UNIV CALIFORNIA; (RAZE-I) RAZ E; (ROMA-I) ROMAN M; (DYNA-N) DYNAVAX
 TECHNOLOGIES CORP
 CYC 83
 PI WO 9855609 A1 19981210 (199907)* EN 49p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
 GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
 UZ VN YU ZW
 AU 9878113 A 19981221 (199919)
 EP 1003850 A1 20000531 (200031) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 US 6225292 B1 20010501 (200126)
 JP 2002505580 W 20020219 (200216) 44p
 US 2002086839 A1 20020704 (200247)
 AU 755322 B 20021212 (200305)
 ADT WO 9855609 A1 WO 1998-US11391 19980605; AU 9878113 A AU 1998-78113
 19980605; EP 1003850 A1 EP 1998-926229 19980605; WO 1998-US11391 19980605;
 US 6225292 B1 Provisional US 1997-48793P 19970606; US 1998-92314 19980605;
 JP 2002505580 W WO 1998-US11391 19980605; JP 1999-502803 19980605; US
 2002086839 A1 Provisional US 1997-48793P 19970606; Cont of US 1998-92314
 19980605; US 2001-770943 20010125; AU 755322 B AU 1998-78113 19980605
 FDT AU 9878113 A Based on WO 9855609; EP 1003850 A1 Based on WO 9855609; JP
 2002505580 W Based on WO 9855609; US 2002086839 A1 Cont of US 6225292; AU
 755322 B Previous Publ. AU 9878113, Based on WO 9855609
 PRAI US 1997-48793P 19970606; US 1998-92314 19980605; US 2001-770943
 20010125
 L25 ANSWER 79 OF 82 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
 AN 1999-06735 BIOTECHDS
 TI Immunostimulatory **CpG** oligodeoxynucleotides enhance the immune
 response to vaccine strategies involving granulocyte-macrophage
 colony-stimulating factor;
 useful for producing an **antigen**-specific TH1 immune response
 e.g. in a tumor **antigen** vaccine
 AU Liu H M; Newbrough S E; Bhatia S K; Dahle C E; Krieg A M; *Weiner G J
 CS Univ.Iowa-Cancer-Cent.; Iowa-City-Verterans-Aff.Med.Cent.
 LO Department of Internal Medicine, University of Iowa, C32K GH, 200 Hawkins
 Dr., Iowa City, IA 52242, USA.
 SO Blood; (1998) 92, 10, 3730-36
 CODEN: BLOOAW ISSN: 0006-4971
 DT Journal
 LA English
 L25 ANSWER 80 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 34
 AN 1998:347908 BIOSIS
 DN PREV199800347908
 TI Bacterial DNA and **immunostimulatory CpG**
oligonucleotides trigger maturation and activation of murine
 dendritic cells.
 AU Sparwasser, Tim; Koch, Eva-Sophie; Vabulas, Ramunas M.; Heeg, Klaus;

FILE 'STNGUIDE' ENTERED AT 12:28:51 ON 14 AUG 2003
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FILE 'CAPLUS' ENTERED AT 12:34:57 ON 14 AUG 2003
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=> d ab 64 65 67 69 79 80

L25 ANSWER 64 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 28

AB Bacterial DNA and synthetic **CpG**-oligodeoxynucleotides (ODNs)
derived thereof have attracted attention because they activate cells of
the immune system in a sequence-dependent manner. Here we investigated the
potential of **CpG**-ODNs to cause proliferation, cytokine
production, and regulation of surface molecules in human B-chronic
lymphocytic leukemia (CLL) cells. **CpG**- ODN induced proliferation
in both B-CLL cells and normal B cells; however, only B-CLL cells
increased proliferative responses when **CpG**-ODN was added to
co-cultures of CD40-ligand transfected mouse fibroblasts (CD40LF) and B
cells. Production of interleukin-6 and tumor necrosis factor was

detectable at borderline levels, using **CpG**-ODN as the only stimulus. In contrast, when **CpG**-ODN was added to co-cultures of B cells and CD40LF, a strong increase in cytokine production occurred in B-CLL cells as well as in normal B cells. The surface molecules CD40, CD58, CD80, CD86, CD54, and MHC class I molecules were up-regulated in B-CLL cells, whereas CD95 expression was not influenced by **CpG**-ODN stimulation. The same pattern of surface molecule regulation was observed in normal B cells, but up-regulation of CD40 was significantly stronger in B-CLL cells. Costimulation with **CpG**-ODN and CD40LF resulted in further up-regulation of CD58, CD80, CD86, and MHC class I molecules. In contrast, CD95 expression induced by CD40-ligation was inhibited by **CpG**-ODN. **CpG**-ODN activated B-CLL cells acquired a strong stimulatory capacity toward T cells in allogeneic mixed lymphocyte reaction. This effect was completely inhibited by a combination of anti-CD80 and anti-CD86 monoclonal antibody. Taken together, these findings suggest the possible use of **CpG**-ODN for immunotherapeutic strategies in patients with B-CLL.

L25 ANSWER 65 OF 82 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
 AB **CpG** DNA, an effective oral adjuvant to protein antigens in mice, was studied. Groups of female BALB/c mice 8-10 weeks were immunized at day 0, 7 and 14 day by oral administration of 100-ug hepatitis B virus surface antigen (HBsAg) or tetanus toxoid (TT), alone or combined with 50, 100, or 500 ug of oligonucleotide containing immunostimulatory (**CpG**) made with a nuclease-resistant phosphorothioate. Control group mice were immunized with 100-ug TT with the non-**CpG** control oligonucleotide. All samples were collected over a 2 day period 1 week after third and final immunization. The results showed that oral delivery of HBsAg without adjuvant resulted in none or only anti-HBs immunoglobulin (Ig) G titers in the plasma of mice. In contrast, much high levels of anti-HBs IgG antibodies were detected when **CpG** was added, with highest titers and lowest variability being obtained with the 100-ug dose. When TT was used as antigen, TT-specific IgG titers in plasma were from 15-20-fold higher than for any of three doses of **CpG** ODN than for TT alone. Results from this study indicate that stimulatory **CpG** ODN may be effective as adjuvant with oral vaccines. (30 ref)

L25 ANSWER 67 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 DUPLICATE 29
 AB Objective. **CpG**-oligodeoxynucleotides (**CpG**-ODN) have been shown to induce proliferation, cytokine production, and surface molecule regulation in normal and malignant human B cells. In the present study, we investigated the potential of **CpG**-ODN to induce functional high-affinity receptors in leukemic and normal B cells and the effects of costimulation with IL-2 on proliferation, cytokine secretion, and surface molecule regulation. Methods. Highly purified B cells from B-CLL patients and normal controls were stimulated with **CpG**-ODN with or without IL-2. Expression of CD25 was determined using FACS, and the presence of high-affinity IL-2 receptors was determined by scatchard analysis. Costimulatory effects of IL-2 and **CpG**-ODN were investigated using proliferation assays, ELISA (IL-6, TNF- α), and FACS analysis (CD80, CD86 expression). Reactivity of autologous and allogeneic T cells toward activated B-CLL cells was determined in mixed lymphocyte reactions and Interferon- γ . Elispot assays. Results. The **CpG**-ODN DSP30 caused a significantly stronger induction of the IL-2 receptor α chain in malignant as compared with normal B cells ($p = 0.03$). This resulted in the expression of functional high-affinity IL-2 receptors in B-CLL cells, but fewer numbers of receptors with less affinity were expressed in normal B cells. Although addition of IL-2 to **CpG**-ODN-stimulated cells augmented proliferation in both normal B cells and B-CLL cells, no costimulatory effect on cytokine production or

surface molecule expression could be observed in normal B cells. In contrast, TNF- α and IL-6 production was increased in B-CLL cells, and the expression of CD80 and CD86 was further enhanced when IL-2 was used as a costimulus. Autologous and allogeneic immune recognition of B-CLL cells stimulated with CpG-ODN and IL-2 was increased compared with B-CLL cells stimulated with CpG-ODN alone. Conclusion. Stimulation of B-CLL cells with CpG-ODN and IL-2 might be an attractive strategy for potential immunotherapies for B-CLL patients. (C) 2000 International Society for Experimental Hematology.

L25 ANSWER 69 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN

AB Initiation of antiviral and anti-tumor T cell responses is probably achieved mainly by dendritic cells (DC) transporting **antigen** from the periphery into organized lymphoid tissues. To develop T cell vaccines it is, therefore, important to understand the accessibility of the **antigen** to DC in vivo and whether DC are activated by vaccination. Here we have evaluated the immunogenicity of a liposomal vaccine formulation with antigenic peptides derived from the glycoprotein of the lymphocytic choriomeningitis virus. Liposome-encapsulated peptides were highly immunogenic when administered intradermally and elicited protective antiviral immunity. After intradermal injection, liposomes formed **antigen** depots which facilitated long-lasting in vivo **antigen** loading of dendritic cells almost exclusively in the local draining lymph nodes. The immunogenicity of the liposomal peptide vaccine was further enhanced by incorporation of **immunostimulatory oligonucleotides** leading to activation of DC. This optimized liposomal peptide vaccine elicited also anti-tumor immunity and induced CTL responses comparable to adoptively transferred, peptide-presenting DC. Thus, our data show that liposomal formulations of peptide vaccines are highly effective at direct in vivo **antigen** loading and activation of DC leading to protective antiviral and anti-tumor immune responses.

L25 ANSWER 79 OF 82 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

AB The 38C12 mouse B-lymphocyte lymphoma system was utilized to study the immune response elicited by a combination of two vaccine adjuvants, granulocyte-macrophage colony stimulating factor (GM-CSF) and **immunostimulatory oligonucleotides** containing the CpG motif (ODN). An enhanced production of **antigen**-specific antibody was seen following s.c. immunization into C3H/HeN mice with both ODN and soluble GM-CSF; and a production shift towards the IgG2a isotype was also found, indicating an enhanced TH1 response. This effect increased following repeat immunizations with ODN and an 38C12 anti-idiotypic mouse GM-CSF fusion protein (FP). Tumor growth was prevented when a single immunization of ODN and the FP was given 3 days prior to tumor inoculation. Bone marrow derived-cells pulsed with the FP and ODN exhibited an increased production of interleukin-12 and major histocompatibility complex class-I and -II. This approach involving the use of ODN in combination with GM-CSF may be useful in tumor immunization protocols and in other therapies where an **antigen**-specific TH1 immune response is required. (38 ref)

L25 ANSWER 80 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 34

AB Bacterial DNA and immunostimulatory (i.s.) synthetic CpG-oligodeoxynucleotides (ODN) act as adjuvants for Th1 responses and cytotoxic T cell responses to proteinaceous antigens. Dendritic cells (DC) can be referred to as "nature's adjuvant" since they display the unique capacity to sensitize naive T cells. Here, we demonstrate that bacterial DNA or i.s. CpG-ODN cause simultaneous maturation of immature DC and activation of mature DC to produce cytokines. These events are associated with the acquisition of professional **antigen**-presenting cell (APC) function. Unfractionated murine bone marrow-derived

DC and FACS-fractionated MHC class II^{low} (termed immature DC) or MHC class II^{high} populations (termed mature DC) were stimulated with bacterial DNA or i.s. **CpG**-ODN. Similar to lipopolysaccharide, i.s. **CpG**-ODN caused up-regulation of MHC class II, CD40 and CD86, but not CD80 on immature and mature DC. In parallel both DC subsets were activated to produce large amounts of IL-12, IL-6 and TNF- α . **CpG**-ODN-activated DC displayed professional APC function in allogeneic mixed lymphocyte reaction and in staphylococcal enterotoxin B-driven naive T cell responses. We interpret these findings to mean that bacterial DNA and i.s. **CpG**-ODN cause maturation (first step) and activation (second step) of DC to bring about conversion of immature DC into professional APC.

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002044337 A5 20020429 AU 2002-44337 20011016

EP 1326638 A2 20030716 EP 2001-987671 20011016

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI GB 1999-8885 A 19990419

US 1999-301829 A2 19990429

WO 2000-EP2920 A2 20000404

GB 2000-25573 A 20001018

GB 2000-25574 A 20001018

US 2000-690921 A 20001018

WO 2001-EP11984 W 20011016

AB The present invention relates to adjuvant compns. which are suitable to be
 used in vaccines. In particular, the adjuvant compn. of the invention
 comprises a saponin and an immunostimulatory oligonucleotide, optionally
 with a carrier. Also provided by the disclosed invention are vaccines
 comprising the adjuvants of the present invention and an antigen. Further
 provided are methods of manuf. of the adjuvants and vaccines of the
 present invention and their use as medicaments. Methods of treating an
 individual susceptible to or suffering from a disease by the
 administration of the vaccines of the present invention are also provided.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 20 MEDLINE on STN DUPLICATE 1

AN 2003365264 IN-PROCESS

DN 22781005 PubMed ID: 12899574

TI Development of RTS,S/AS02: a purified subunit-based
malaria vaccine candidate formulated with a novel adjuvant.

AU **Garcon Nathalie**; Heppner D Gray; Cohen Joe

CS Research & Development, GlaxoSmithKline Biologicals, Rixensart, Belgium..
 nathalie.garcon@gskbio.com

SO Expert Rev Vaccines, (2003 Apr) 2 (2) 231-8.

Journal code: 101155475. ISSN: 1476-0584.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS IN-PROCESS; NONINDEXED; Priority Journals

ED Entered STN: 20030806

Last Updated on STN: 20030806

AB During the past decade, tremendous progress has been made in process
 development allowing for the production of large quantities of recombinant
 antigens, as well as in the understanding of the immune mechanisms
 underlying protection. Parallel to this, various and numerous adjuvant
 systems have been developed and tested in animal models and in clinical
 trials but have rarely induced protection. This review will discuss the
 development of a new adjuvant system (AS02) in combination with a
malaria vaccine antigen candidate. To date, this vaccine is the
 only one to demonstrate protection in man in artificial challenge as well
 as in natural field trials. It has been established that this adjuvant
 system is capable of eliciting high antibody titers along with strong
 cell-mediated immunity which both contribute to the efficacy of the
 vaccine.

L9 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:574951 CAPLUS

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1198243 A2 20020424 EP 2000-945810 20000623

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL

PRAI GB 1999-15204 A 19990629

WO 2000-EP5841 W 20000623

AB A vaccine formulation for the prevention or amelioration of
plasmodium infection in humans is provided. The vaccine comprises
 a **malaria** antigen, esp. a protein which comprises a portion of
 the CS protein of *P. falciparum* fused in frame via a linear linker to the
 N-terminal of HBsAg, and an immunostimulatory CpG oligonucleotide.
 Methods for making the vaccine formulation of the invention are described.
 Patients may also be treated by pre-administration of the CpG
 oligonucleotide prior to administration of the **malaria** antigen.

L9 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2001:922287 CAPLUS

DN 137:31752

TI Efficacy of **RTS,S/AS02 malaria** vaccine against
Plasmodium falciparum infection in semi-immune adult men in
 Gambia: A randomized trial

AU [Bojang, Kalifa A.; Milligan, Paul J. M.; Pinder, Margaret; Vigneron,
 Laurence; Allouche, Ali; Kester, Kent E.; Ballou, W. Ripley; Conway,
 David J.; Reece, William H. H.; Gothard, Philip; Yamuah, Lawrence;
 Delchambre, Martine; Voss, Gerald; Greenwood, Brian M.; Hill,
 Adrian; McAdam, Keith P. W. J.; Tornieporth, Nadia; Cohen, Joe D.;
 Doherty, Tom

CS RTS, S Malaria Vaccine Trial Team, Medical Research Council Laboratories,
 Banjul, Gambia

SO [Lancet (2001), 358(9297), 1927-1934 /
 CODEN: LANCAO; ISSN: 0140-6736

PB Lancet Ltd.

DT Journal

LA English

AB Background: **RTS,S/AS02** is a pre-erythrocytic **malaria**
 vaccine based on the circumsporozoite surface protein of
Plasmodium falciparum fused to HBsAg, incorporating a new adjuvant
 (AS02). We did a randomized trial of the efficacy of **RTS,S/AS02**
 against natural *P falciparum* infection in semi-immune adult men in Gambia.
 Methods: 306 men aged 18-45 yr were randomly assigned three doses of
 either **RTS,S/AS02** or rabies vaccine (control). Volunteers were
 given sulfadoxine/pyrimethamine 2 wk before dose 3, and kept under
 surveillance throughout the **malaria** transmission season. Blood
 smears were collected once a week and whenever a volunteer developed
 symptoms compatible with **malaria**. The primary endpoint was time
 to first infection with *P falciparum*. Anal. was per protocol. Findings:
 250 men (131 in the **RTS,S/AS02** group and 119 in the control
 group) received three doses of vaccine and were followed up for 15 wk.
RTS,S/AS02 was safe and well tolerated. *P falciparum* infections
 occurred significantly earlier in the control group than the **RTS**
,S/AS02 group. Vaccine efficacy, adjusted for confounders, was 34%.
 Protection seemed to wane: estd. efficacy during the first 9 wk of
 follow-up was 71% (46-85), but decreased to 0% (-52 to 34) in the last 6
 wk. Vaccination induced strong antibody responses to circumsporozoite
 protein and strong T-cell responses. Protection was not limited to the
 NF54 parasite genotype from which the vaccine was derived. 158 Men
 received a fourth dose the next year and were followed up for 9 wk; during

this time, vaccine efficacy was 47% (4-71). Interpretation: **RTS**, S/AS02 is safe, immunogenic, and is the first pre-erythrocytic vaccine to show significant protection against natural P falciparum infection.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2001:181200 BIOSIS
DN PREV200100181200
TI Efficacy of recombinant circumsporozoite protein vaccine regimens against experimental **Plasmodium falciparum malaria**.
AU Kester, Kent E. (1); McKinney, Denise A.; Tornieporth, Nadia; Ockenhouse, Christian F.; Heppner, D. Gray; Hall, Ted; Krzych, Urszula; Delchambre, Martine; **Voss, Gerald**; Dowler, Megan G.; Palensky, Jolie; Wittes, Janet; Cohen, Joe; Ballou, W. Ripley
CS (1) Dept. of Immunology, Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD, 20910: kent.kester@na.amedd.army.mil USA
SO Journal of Infectious Diseases, (15 February, 2001) Vol. 183, No. 4, pp. 640-647. print.
ISSN: 0022-1899.
DT Article
LA English
SL English
AB After initial successful evaluation of the circumsporozoite-based vaccine **RTS,S/SBAS2**, developed by SmithKline Beecham Biologicals with the Walter Reed Army Institute of Research, protective efficacy of several regimens against **Plasmodium falciparum** challenge was determined. A controlled phase 1/2a study evaluated 1 or 2 standard doses of **RTS,S/SBAS2** in 2 groups whose members received open-label therapy and 3 immunizations in blinded groups who received standard, one-half, or one-fifth doses. **RTS,S/SBAS2** was safe and immunogenic in all groups. Of the 41 vaccinees and 23 control subjects who underwent sporozoite challenge, **malaria** developed in 7 of 10 who received 1 dose, in 7 of 14 who received 2 doses, in 3 of 6 who received 3 standard doses, in 3 of 7 who received 3 one-half doses, in 3 of 4 who received 3 one-fifth doses, and in 22 of 23 control subjects. Overall protective efficacy of **RTS,S/SBAS2** was 41% (95% confidence interval, 22%-56%; P = .0006). This and previous studies have shown that 2 or 3 doses of **RTS,S/SBAS2** protect against challenge with P. falciparum sporozoites.

L9 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:756545 CAPLUS
DN 133:340220
TI Adjuvant comprising a saponin and an immunostimulatory oligonucleotide for manufacture of vaccines
IN Friede, Martin; **Garcon, Nathalie**; Hermand, Philippe
PA Smithkline Beecham Biologicals S. A., Belg.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000062800	A2	20001026	WO 2000-EP2920	20000404
	WO 2000062800	A3	20010111		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,

	US 2003095974	A1	20030522	US 2002-139815	20020506
PRAI	GB 1997-18902	A	19970905		
	GB 1997-20982	A	19971002		
	EP 1998-954264	A3	19980902		
	WO 1998-EP5715	W	19980902		
	US 2000-486997	B1	20000731		

AB The present invention relates to an oil-in-water emulsion vaccine compn. In particular, the present invention relates to a vaccine adjuvant formulation based on oil-in-water emulsion comprising a metabolizable oil and a saponin, wherein the oil and a saponin are present in a ratio of between 1:1 and 200:1. The invention further relates to methods for prepg. the emulsion and its use in medicine. The preferred saponin is Quila or deriv. thereof, such as QS21 and the preferred oil is squalene.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2000:15300 BIOSIS
DN PREV200000015300
TI Potent induction of focused Th1-type cellular and humoral immune responses by RTS,S/SBAS2, a recombinant **Plasmodium falciparum** malaria vaccine.
AU Lalvani, Ajit (1); Moris, Phillipe; Voss, Gerald; Pathan, Ansar A.; Kester, Kent E.; Brookes, Roger; Lee, Edwin; Koutsoukos, Marguerite; Plebanski, Magdalena; Delchambre, Martine; Flanagan, Katie L.; Carton, Cecile; Slaoui, Moncef; Van Hoecke, Christian; Ballou, W. Ripley; Hill, Adrian V. S.; Cohen, Joe
CS (1) Nuffield Dept. of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Level 7, Oxford, OX3 9DU UK
SO Journal of Infectious Diseases, (Nov., 1999)-Vol. 180, No. 5, pp. 1656-1664.
ISSN: 0022-1899.

DT Article
LA English
SL English

AB The RTS,S/SBAS2 vaccine confers sterile protection against **Plasmodium falciparum** sporozoite challenge. The mechanisms underlying this are of great interest, yet little is known about the immune effector mechanisms induced by this vaccine. The immune responses induced by RTS,S/SBAS2 were characterized in 10 malaria-naive volunteers. Several epitopes in the circumsporozoite protein (CSP) were identified as targets of cultured interferon (IFN)-gamma-secreting CD4+ T cells. RTS,S-specific IFN-gamma-secreting effector T cells were induced in 8 subjects; this ex vivo response mapped to a single peptide in Th2R. CSP-specific CD8+ cytotoxic T lymphocytes were not detected. RTS,S-specific IFN-gamma production was universal, whereas interleukin-4 and -5 production was rare. RTS,S-specific lymphoproliferative responses and antibodies to CSP were strongly induced in all volunteers. Responses waned with time but were boostable. Thus, RTS,S/SBAS2 is a potent inducer of Th1-type cellular and humoral immunity. These results highlight possible immune mechanisms of protection and have important implications for vaccine design in general.

L9 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:7854 CAPLUS
DN 130:57241
TI Oil-in-water vaccine compositions
IN Garcon, Nathalie; Momin, Patricia Marie Christine Aline Francoise
PA Smithkline Beecham Biologicals S.A., Belg.
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2

PRAI GB 1996-16351 A 19960802
WO 1997-EP4326 W 19970731
US 1999-230629 B1 19990401
US 2001-826213 A1 20010405
US 2001-826513 B1 20010405
US 2001-24860 B1 20011218

AB A vaccine compn. useful in the prevention or treatment of **malaria** comprises a plurality of **malaria**-derived antigens in combination with an adjuvant which is a preferential stimulator of TH1 cell response.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:70559 BIOSIS
DN PREV199799369762
TI A preliminary evaluation of a recombinant circumsporozoite protein vaccine against **Plasmodium falciparum malaria**.
AU [Stoute, Jose A.; Slaoui, Moncef; Heppner, D. Gray; Momin, Patricia; Kester, Kent E.; Desmons, Pierre; Wellde, Bruce T.; **Garcon, Nathalie**; Krzych, Urszula; Marchand, Martine; Ballou, W. Ripley (1); Cohen, Joe D.
CS (1) Dep. Immunol., Walter Reed Army Inst. Res., Washington, DC 20307-5100 USA
SO New England Journal of Medicine, (1997) Vol. 336, No. 2, pp. 86-99.
ISSN: 0028-4793.

DT Article

LA English

AB Background: The candidate vaccines against **malaria** are poorly immunogenic and thus have been ineffective in preventing infection. We developed a vaccine based on the circumsporozoite protein of **Plasmodium falciparum** that incorporates adjuvants selected to enhance the immune response. Methods: The antigen consists of a hybrid in which the circumsporozoite protein fused to hepatitis B surface antigen (HBsAg) is expressed together with unfused HBsAg. We evaluated three formulations of this antigen in an unblinded trial in 46 subjects who had never been exposed to **malaria**. Results: Two of the vaccine formulations were highly immunogenic. Four subjects had adverse systemic reactions that may have resulted from the intensity of the immune response after the second dose, which led us to reduce the third dose. Twenty-two vaccinated subjects and six unimmunized controls underwent a challenge consisting of bites from mosquitoes infected with *P. falciparum*. **Malaria** developed in all six control subjects, seven of eight subjects who received vaccine 1, and five of seven subjects who received vaccine 2. In contrast, only one of seven subjects who received vaccine 3 became infected (relative risk of infection, 0.14; 95 percent confidence interval, 0.02 to 0.88; *P* lt 0.005). Conclusions: A recombinant vaccine based on fusion of the circumsporozoite protein and HBsAg plus a potent adjuvant can protect against experimental challenge with *P. falciparum* sporozoites. After additional studies of protective immunity and the vaccination schedule, field trials are indicated for this new vaccine against *P. falciparum malaria*.

L9 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:493517 CAPLUS

DN 119:93517

TI Hybrid protein with **Plasmodium** CS protein sequence and hepatitis B surface antigen sequence, and use for vaccine against **malaria**

IN De Wilde, Michel; **Cohen, Joseph**

PA Smithkline Beecham Biologicals S.A., Belg.

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent

LA English

- (4) immunizing or treating an animal by:
 - (a) administering the vaccine to the animal;
 - (b) priming a T cell response in the animal by administering the vaccine; or
 - (c) boosting a T cell response in the animal by administering the vaccine.

ACTIVITY - Immunostimulant; Cytostatic; Antiallergic; Virucide; Antibacterial.

Mice were subcutaneously primed with 100 micro g p33-VLP alone, mixed with 20 nmol **CpG**-oligonucleotide (p33-VLP+**CpG**), or p33-VLP packaged with **CpG**-oligonucleotide after dialysis of free **CpG**-oligonucleotide (p33-VLP/**CpG**). Untreated naive mice served as negative control. Twenty days later, mice were challenged with lymphocytic choriomeningitis virus (LCMV) (200 plaque forming units (pfu)), intravenously). Results showed that LCMV titer (log10) was lowest for p33-VLP/**CpG**.

MECHANISM OF ACTION - Vaccine.

USE - The composition is useful as a vaccine for enhancing an immune response in an animal, particularly a mammal or human. Specifically, the composition is useful for enhancing a B cell response, a T cell response (particularly a Th or Th1 cell response), or a cytotoxic T-lymphocyte (CTL) response. (All claimed.) The composition or vaccine is also useful for immunizing or treating an animal (claimed), e.g. humans, sheep, horses, cattle, pigs, dogs, cats, rats, birds, reptiles or fish. The composition is particularly useful as prophylactic or therapeutic vaccines against allergies, tumors (e.g. breast cancers, neuroblastoma, or leukemia), viral diseases (e.g. influenza, hepatitis, measles or chicken pox), or bacterial infections (e.g. tuberculosis, pneumonia or syphilis).
Dwg.0/55

L14 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 1

AN 2002:529252 BIOSIS

DN PREV200200529252

TI **CpG** oligodeoxynucleotides induce human monocytes to mature into functional dendritic cells.

AU Gursel, Mayda; Verthelyi, Daniela; Klinman, Dennis M. (1)

CS (1) Section of Retroviral Immunology, Center for Biologics Evaluation and Research, Food and Drug Administration, Bldg 29A Rm 3 D 10, CBER/FDA, Bethesda, MD, 20892: Klinman@CBER.FDA.GOV USA

SO European Journal of Immunology, (September, 2002) Vol. 32, No. 9, pp. 2617-2622. <http://www.wiley-vch.de/publish/en/journals/alphabeticIndex/2040/?sID=87ce709e9d93384f19ebcbf2d13f6116>. print.

ISSN: 0014-2980.

DT Article

LA English

AB Dendritic cells (DC) excel at presenting **antigen** to T cells and thus make a key contribution to the induction of primary and secondary immune responses. DC matured in vitro and pulsed with **antigen** show promise for the immunotherapy of cancer and infectious diseases. Synthetic **oligonucleotides** (ODN) expressing **immunomodulatory** "**CpG** motifs" were found to boost APC function in mice. Current results demonstrate that the recently identified "D" type of **CpG** ODN stimulate human peripheral blood monocytes to mature into functionally active DC over 2-4 days. The transition from monocyte to DC is characterized by the up-regulation of CD83, CD86, CD80, CD40 and the down-regulation of CD14. These DC support **antigen**-specific humoral and cellular responses in vitro and in vivo. The differentiation of these monocytes is mediated by plasmacytoid DC, which respond to D type ODN by secreting IFN-alpha. Since D type **CpG** motifs are present in bacterial and viral DNA, the maturation of monocytes into functional DC may reflect a physiologic response that can be harnessed therapeutically through the use of **CpG** ODN.

L14 ANSWER 4 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 2002216433 EMBASE
 TI Towards optimal design of second-generation immunomodulatory
 oligonucleotides.
 AU Kandimala E.R.; Yu D.; Agrawal S.
 CS S. Agrawal, Hybridon Inc., 345 Vassar Street, Cambridge, MA 02139, United
 States. sagrawal@hybridon.com
 SO Current Opinion in Molecular Therapeutics, (2002) 4/2 (122-129).
 Refs: 58
 ISSN: 1464-8431 CODEN: CUOTFO
 CY United Kingdom
 DT Journal; Article
 FS 022 Human Genetics
 026 Immunology, Serology and Transplantation
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 039 Pharmacy
 LA English
 SL English
 AB The goal of using of oligodeoxyribonucleotides containing CpG
 dinucleotides (CpG DNA) as immunomodulatory agents has been
 realized in recent years. Therapeutic applications of CpG DNA as
 monotherapies and as adjuvants in combination with vaccines, antibodies,
 antigens and allergens for a number of disease indications are rapidly
 expanding, and the safety and efficacy of several first-generation
 CpG DNA agents are being evaluated in human clinical trials. The
 biological effects of CpG DNA have been known for two decades;
 however, only recently has a specific receptor(s) that recognizes
 CpG DNA and activates immune cascade been identified. A number of
 sequence and structural characteristics of CpG DNA and chemical
 modifications that influence immunostimulatory activity have been
 identified. In this article we summarize the recent progress in
 understanding the structural and chemical characteristics of CpG
 DNA that are significant for molecular recognition. In addition, we
 describe the design of second-generation CpG DNA agents, and
 clinical application of first-generation agents.

L14 ANSWER 5 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 2000-524416 [47] WPIDS
 CR 1997-145245 [13]; 1997-319766 [29]; 1998-101069 [09]; 1998-609243 [51];
 1999-263358 [22]; 1999-313351 [26]; 2000-587434 [55]; 2000-594650 [56];
 2001-050094 [06]; 2002-083006 [11]; 2002-393965 [42]; 2003-182286 [18]
 DNC C2000-155775
 TI Novel methods for obtaining polynucleotides with optimized
 immunomodulatory responses by directed evolution.
 DC B04 C06 D16
 IN SHORT, J M
 PA (DIVE-N) DIVERSA CORP
 CYC 90
 PI WO 2000046344 A2 20000810 (200047)* EN 716p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
 FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
 LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
 TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
 AU 2000034839 A 20000825 (200059)
 EP 1073710 A2 20010207 (200109) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 ADT WO 2000046344 A2 WO 2000-US3086 20000204; AU 2000034839 A AU 2000-34839

fusion protein optionally linked to an immunological fusion partner, and an **immunomodulatory CpG oligonucleotide**.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The composition can be used to induce an immune response in a patient to an HPV **antigen**. It can also be used for preventing or treating HPV induced tumors (all claimed).

ADVANTAGE - None given.

Dwg.0/6

L14 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1998:158397 BIOSIS
DN PREV199800158397
TI **Immunomodulatory** effects of **CPG**-based
oligonucleotides (OLIGOS) patterned after sequences present in
bacterial DNA.
AU Klinman, Dennis M. (1)
CS (1) Cent. Biol., FDA, Bethesda, MD 20892 USA
SO Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S276
Meeting Info.: 61st National Scientific Meeting of the American College of
Rheumatology and the 32nd National Scientific Meeting of the Association
of Rheumatology Health Professionals Washington, DC, USA November 8-12,
1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.
DT Conference
LA English

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	ENTRY	SESSION
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	ENTRY	SESSION
FULL ESTIMATED COST	0.06	150.92
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-14.32

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FILE 'EMBASE' ENTERED AT 12:15:56 ON 14 AUG 2003
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molecule that improves the transport or presentation of antigens by a cell, comprising screening a library of non-stochastically generated polynucleotides optimized (for a human or animal) by directed evolution as in (I), for a polynucleotide that encodes a recombinant molecule that modulates antigen transport or presentation;

(4) obtaining an immunomodulatory polynucleotide with optimized expression in a host comprising creating an optimized non-stochastically generated polynucleotide library as in (I);

(5) obtaining an immunomodulatory polynucleotide with optimized expression in a host comprising creating and optionally screening a library an optimized non-stochastically generated polynucleotide library;

(6) producing a progeny polynucleotide set comprising:

(a) annealing 2 primers to a circular parental polynucleotide, where the annealment regions of the polynucleotides are non-overlapping and 1 of the primers contains a non-stochastic mutagenic (optionally degenerate) cassette; and

(b) synthesizing a progeny polynucleotide for each primer by a polymerase-catalyzed amplification reaction, where the progeny polynucleotides may form a double-stranded mutagenized circular polynucleotide;

(7) producing progeny polypeptides containing a non-stochastic range of single amino acid substitutions from a template polypeptide, and optionally identifying desirable amino acid substitutions and combinations, comprising:

(a) amplifying a codon-containing template polynucleotide using a degenerate oligonucleotide for each codon to be mutated, where each oligonucleotide comprises a homologous sequence and (at least 1) degenerate trinucleotide cassette;

(b) subjecting the resultant progeny polynucleotides to clonal amplification to express the encoded polypeptides; and optionally

(c) screening the progeny to identify those with a desirable change in at least 1 molecular property compared to the parent polynucleotide.

USE - The methods are useful for obtaining polynucleotide and polypeptides that can be used as genetic vaccines in the immunomodulation of humans and animals. The polynucleotides and peptides are preferably used as vaccines in the treatment, prevention or diagnosis of malaria. The methods are also useful for producing polynucleotides and/or polypeptides with enhanced (biological) properties, e.g. increased stability ex vivo (for increased shelf-life and ease of storage), stability in vivo (increased resistance to digestive acids and increased stability in circulation) (claimed), thermostable enzymes, improved vector transfer efficiency, improved immunogenicity, host (e.g. human) optimized vaccine (claimed) and targeted sequences.

Dwg.0/42

L15 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2001:22180 CAPLUS

DN 134:206253

TI How do you see CG?

AU Aderem, Alan; Hume, David A.

CS Institute for Systems Biology, Seattle, WA, USA

SO Cell (Cambridge, Massachusetts) (2000), 103(7), 993-996

CODEN: CELLB5; ISSN: 0092-8674

PB Cell Press

DT Journal; General Review

LA English

AB A review with 20 refs. about the **immunomodulatory** effects of

CpG-oligonucleotides. Topics discussed include

toll-like receptor 9 and its signaling pathway in response to **CpG**

-oligonucleotides; DNA-dependent protein kinase in response to **CpG**

-oligonucleotides; and mechanism by which TLR9 and DNS-PK might interact.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 1286 S CPG AND ADJUVANT
 L17 513 DUP REM L16 (773 DUPLICATES REMOVED)
 L18 216 S L17 AND IMMUNOSTIMULAT?
 L19 19 S L18 AND (MALARIA OR PLASMODIUM OR RTS OR TRAP OR HYBRID)

=> d bib ab 119 1-19

L19 ANSWER 1 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2000:447456 BIOSIS
 DN PREV200000447456
 TI **CpG** DNA as a Th1-promoting **adjuvant** in immunization
 against Trypanosoma cruzi.
 AU Corral, Ricardo S. (1); Petray, Patricia B.
 CS (1) Laboratorio de Virologia, Hospital de Ninos Ricardo Gutierrez, Gallo
 1330, 1425, Buenos Aires Argentina
 SO Vaccine, (15 September, 2000) Vol. 19, No. 2-3, pp. 234-242. print?
 ISSN: 0264-410X.
 DT Article
 LA English
 SL English
 AB Th1-type immune response plays a critical role in resistance to
 Trypanosoma cruzi infection. We asked whether a synthetic
 oligodeoxynucleotide that contains **immunostimulatory CpG**
 motifs (**CpG** ODN), known to promote a Th1 response, could act as
 an **adjuvant** in immunization with parasite antigens. Mice
 immunized with a whole homogenate (WH) of T. cruzi antigens
 co-administered with **CpG** ODN presented high titers of T. cruzi
 antibodies (IgG2a isotype), strong delayed type hypersensitivity and a
 Th1-dominated (IFN-gamma and IL-12) cytokine profile. Furthermore, WH plus
CpG ODN protected mice from challenge with an otherwise lethal
 dose of bloodstream trypomastigotes. As reported for leishmaniasis and
malaria, **CpG** ODN holds considerable promise as an
adjuvant for future vaccines against T. cruzi.

L19 ANSWER 2 OF 19 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1999:417071 BIOSIS
 DN PREV199900417071
 TI Synthetic oligodeoxynucleotides containing **CpG** motifs enhance
 immunogenicity of a peptide **malaria** vaccine in Aotus monkeys.
 AU Jones, Trevor R. (1); Obaldia, Nicanor, III; Gramzinski, Robert A.;
 Charoenvit, Yupin; Kolodny, Nelly; Kitov, Svetlana; Davis, Heather L.;
 Krieg, Arthur M.; Hoffman, Stephen L.
 CS (1) Malaria Program, Naval Medical Research Center, Bethesda, MD USA
 SO Vaccine, (Aug. 6, 1999) Vol. 17, No. 23-24, pp. 3065-3071.
 ISSN: 0264-410X.
 DT Article
 LA English
 SL English
 AB Synthetic peptide and recombinant protein vaccines are optimally
 immunogenic when delivered with an effective **adjuvant**. Candidate
 vaccines currently insufficiently immunogenic may induce a protective
 immunity if they could be delivered with more effective adjuvants. For
 example, immunogens that induce promising responses when administered to
 mice with complete and incomplete Freund's adjuvants perform less well in
 primate animal models where complete Freund's **adjuvant** is not
 used. We report the use of synthetic oligodeoxynucleotides containing
CpG motifs, the sequences of which are based on
immunostimulatory bacterial DNA sequences, to enhance the immune
 response in Aotus monkeys to a synthetic peptide **malaria**
 vaccine. Monkeys were immunized with the synthetic peptide PADRE 45, a
 synthetic peptide containing amino acid sequences derived from the
 circumsporozoite protein (CSP) from **Plasmodium falciparum**, and
 delivered in an emulsion of saline and Montanide 720, a mannide oleate in

669-72. Ref: 10
Journal code: 2984781R. ISSN: 0047-1860.

CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA Japanese
FS Priority Journals
EM 200110

ED Entered STN: 20010827
Last Updated on STN: 20011022
Entered Medline: 20011018

AB DNA vaccine involves the injection of plasmid DNA encoding an antigen under the control of an eukaryotic promoter, and results in cellular and humoral immune responses to the plasmid DNA-encoded antigen. The immune response induced by DNA vaccine usually has a T-helper-1(Th1) bias through a potent Th1-promoting **adjuvant** effect of **immunostimulatory** DNA sequences with **CpG** motifs present in plasmid DNA. It has been demonstrated that volunteers who were vaccinated with plasmid DNA encoding a **malaria** protein or a human immunodeficiency virus protein developed antigen-specific, human leukocyte antigen(HLA)-restricted, CD8+ cytotoxic T lymphocytes(CTLs) The demonstration in humans of the induction of CD8+ CTLs by DNA vaccines, including CTLs, provides a foundation for further clinical application of this potentially revolutionary vaccine technology.

L19 ANSWER 5 OF 19 MEDLINE on STN

AN 2000318758 MEDLINE

DN 20318758 PubMed ID: 10861094

TI Repeated administration of cytosine-phosphorothiolated guanine-containing oligonucleotides together with peptide/protein immunization results in enhanced CTL responses with anti-tumor activity.

AU Davila E; Celis E

CS Department of Immunology, Mayo Clinic and Mayo Graduate School, Rochester, MN 55905, USA.

NC R01CA80782 (NCI)

R01CA82677 (NCI)

SO JOURNAL OF IMMUNOLOGY, (2000 Jul 1) 165 (1) 539-47

Journal code: 2985117R. ISSN: 0022-1767.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200007

ED Entered STN: 20000811

Last Updated on STN: 20000811

Entered Medline: 20000731

AB The development of therapeutic anti-cancer vaccines designed to elicit CTL responses with anti-tumor activity has become a reality thanks to the identification of several tumor-associated Ags and their corresponding peptide T cell epitopes. However, peptide-based vaccines, in general, fail to elicit sufficiently strong CTL responses capable of producing therapeutic anti-tumor effects (i.e., prolongation of survival, tumor reduction). Here we report that repeated administration of synthetic oligonucleotides containing foreign cytosine-phosphorothiolated guanine (**CpG**) motifs increased 10- to 100-fold the CTL response to immunization with various synthetic peptides corresponding to well-known T cell epitopes. Moreover, repeated **CpG** administration allowed the induction of CTL to soluble protein even in the absence of additional **adjuvant**. Our results indicate that the potentiating effect of **CpG** in CTL responses required the participation of Th lymphocytes. Repeated **CpG** administration resulted in overt splenomegaly and lymphadenopathy with a significant increase in the numbers of CTL

Animal protection studies suggest that synergistic combinations of cytokines and immunomodulating molecules may be required to protect from a viral challenge. For example, GM-CSF has been shown to be synergistic with IL-12 or CD40 ligand for induction of CTL and for antiviral protection, and the triple combination of GM-CSF, IL-12, and TNF alpha appears to induce the most effective protection in some mouse models. Chemokine-antigen fusions have also been shown to enhance immunogenicity of the antigen. Combinations of costimulatory molecules have been found to be synergistic when incorporated in a vaccine. Combined use of newer more potent vaccine constructs, containing codon optimized epitopes, relevant CpG motifs, cytokines, costimulatory molecules and chemokines, used in heterologous prime-boost strategies with viral vector vaccines or recombinant proteins, might afford the most potent vaccine approaches yet developed. In this review we will discuss the application and delivery of cytokines, costimulatory molecules, and chemokines toward improving current vaccine strategies.

L19 ANSWER 10 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 1998390444 EMBASE
 TI **Immunostimulatory CpG** oligodeoxynucleotides enhance the immune response to vaccine strategies involving granulocyte-macrophage colony-stimulating factor.
 AU Liu H.-M.; Newbrough S.E.; Bhatia S.K.; Dahle C.E.; Krieg A.M.; Weiner G.J.
 CS Dr. G.J. Weiner, Department of Internal Medicine, University of Iowa, 200 Hawkins Dr, Iowa City, IA 52242, United States
 SO Blood, (15 Nov 1998) 92/10 (3730-3736).
 Refs: 38
 ISSN: 0006-4971 CODEN: BLOOAW
 CY United States
 DT Journal; Article
 FS 016 Cancer
 025 Hematology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 LA English
 SL English
 AB **Immunostimulatory** oligodeoxynucleotides containing the **CpG** motif (**CpG** ODN) can activate various immune cell subsets and induce production of a number of cytokines. Prior studies have demonstrated that both **CpG** ODN and granulocyte-macrophage colony-stimulating factor (GM-CSF) can serve as potent vaccine adjuvants. We used the 38C13 murine lymphoma system to evaluate the immune response to a combination of these two adjuvants. Immunization using antigen, **CpG** ODN, and soluble GM-CSF enhanced production of antigen-specific antibody and shifted production towards the IgG2a isotype, suggesting an enhanced TH1 response. This effect was most pronounced after repeat immunizations with **CpG** ODN and antigen/GM-CSF fusion protein. A single immunization with **CpG** ODN and antigen/GM-CSF fusion protein 3 days before tumor inoculation prevented tumor growth. **CpG** ODN enhanced the production of interleukin-12 by bone marrow-derived dendritic cells and increased expression of major histocompatibility complex class I and class II molecules, particularly when cells were pulsed with antigen/GM-CSF fusion protein. We conclude that the use of **CpG** ODN in combination with strategies involving GM-CSF enhances the immune response to antigen and shifts the response towards a TH1 response and that this approach deserves further evaluation in tumor immunization approaches and other conditions in which an antigen-specific TH1 response is desirable.

L19 ANSWER 11 OF 19 CABA COPYRIGHT 2003 CABI on STN
 AN 2001:2967 CABA
 DN 20000810697

TI **CpG** DNA as a Th1-promoting **adjuvant** in immunization
 against *Trypanosoma cruzi*
 AU Corral, R. S.; Petray, P. B.
 CS Laboratorio de Virologia, Hospital de Ninos Ricardo Gutierrez, Gallo 1330,
 1425 Buenos Aires, Argentina.
 SO Vaccine, (2001) Vol. 19, No. 2/3, pp. 234-242. 42 ref.
 ISSN: 0264-410X
 DT Journal
 LA English
 AB Th1-type immune response plays a critical role in resistance to
Trypanosoma cruzi infection. We asked whether a synthetic
 oligodeoxynucleotide that contains **immunostimulatory CpG**
 motifs (**CpG** ODN), known to promote a Th1 response, could act as
 an **adjuvant** in immunization with parasite antigens. Mice
 immunized with a whole homogenate (WH) of *T. cruzi* antigens
 co-administered with **CpG** ODN presented high titres of *T. cruzi*
 antibodies (IgG2a isotype), strong delayed type hypersensitivity and a
 Th1-dominated (IFN- gamma and IL-12) cytokine profile. Furthermore, WH
 plus **CpG** ODN protected mice from challenge with an otherwise
 lethal dose of bloodstream trypomastigotes. As reported for leishmaniasis
 and **malaria**, **CpG** ODN holds considerable promise as an
adjuvant for future vaccines against *T. cruzi*.

L19 ANSWER 12 OF 19 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 2002-130570 [17] WPIDS
 DNC C2002-040090
 TI New **immunostimulatory** compositions comprising RNA/DNA
hybrid oligonucleotides, useful for enhancing an immune response
 or inducing cytokines, particularly for treating diseases, e.g. cancer,
 allergy or HIV infection.
 DC B04 D16
 IN FLORA, M; KLINMAN, D M; MOND, J J
 PA (BIOS-N) BIOSYNEXUS INC
 CYC 96
 PI WO 2001093902 A2 20011213 (200217)* EN 68p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
 SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
 AU 2001075294 A 20011217 (200225)
 EP 1292331 A2 20030319 (200322) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 ADT WO 2001093902 A2 WO 2001-US18276 20010607; AU 2001075294 A AU 2001-75294
 20010607; EP 1292331 A2 EP 2001-941989 20010607, WO 2001-US18276 20010607
 FDT AU 2001075294 A Based on WO 200193902; EP 1292331 A2 Based on WO 200193902
 PRAI US 2000-209797P 20000607
 AB WO 200193902 A UPAB: 20020313
 NOVELTY - An **immunostimulatory** composition, which comprises at
 least one oligonucleotide comprising both an RNA region and a DNA region,
 is new. At least one terminus of the oligonucleotide comprises RNA.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:
 (1) an **adjuvant** comprising the **immunostimulatory**
 composition;
 (2) vaccines (I) comprising:
 (a) at least one oligonucleotide comprising both an RNA region and a
 DNA region, where at least one terminus of the oligonucleotide comprises
 RNA, where the oligonucleotide is associated with a physiological carrier
 or delivery system;
 (b) at least one oligonucleotide comprising both an RNA region and a

AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 WO 2002032450 A2 20020425 WO 2001-EP11984 20011016
 WO 2002032450 A3 20021010

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002044337 A5 20020429 AU 2002-44337 20011016
 EP 1326638 A2 20030716 EP 2001-987671 20011016
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI GB 1999-8885 A 19990419
 US 1999-301829 A2 19990429
 WO 2000-EP2920 A2 20000404
 GB 2000-25573 A 20001018
 GB 2000-25574 A 20001018
 US 2000-690921 A 20001018
 WO 2001-EP11984 W 20011016

AB The present invention relates to adjuvant compns. which are suitable to be
 used in vaccines. In particular, the adjuvant compn. of the invention
 comprises a saponin and an **immunostimulatory**
oligonucleotide, optionally with a carrier. Also provided by the
 disclosed invention are vaccines comprising the adjuvants of the present
 invention and an **antigen**. Further provided are methods of
 manuf. of the adjuvants and vaccines of the present invention and their
 use as medicaments. Methods of treating an individual susceptible to or
 suffering from a disease by the administration of the vaccines of the
 present invention are also provided.

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 82 MEDLINE on STN DUPLICATE 4
 AN 2003341668 IN-PROCESS
 DN 22756056 PubMed ID: 12874017
 TI **CpG** oligodeoxynucleotides enhance the capacity of
 adenovirus-mediated CD154 gene transfer to generate effective B-cell
 lymphoma vaccines.
 AU Rieger Roman; Kipps Thomas J
 CS Division of Hematology/Oncology, Department of Medicine, University of
 California, San Diego, La Jolla, California 92093-0663, USA.
 NC P01-CA81534 (NCI)
 SO CANCER RESEARCH, (2003 Jul 15) 63 (14) 4128-35.
 Journal code: 2984705R. ISSN: 0008-5472.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS IN-PROCESS; NONINDEXED; Priority Journals
 ED Entered STN: 20030723
 Last Updated on STN: 20030731
 AB Activation of CD40 by CD154 induces **antigen**-presenting cells
 (APC) to express immune costimulatory molecules, thereby enhancing their
 APC activity. **Oligonucleotides** (ODN), containing
immunostimulatory DNA sequences (ISS) with nonmethylated
CpG dinucleotides in a defined motif, also can induce similar
 changes in APC. In this study, we examined whether infection with

recombinant adenovirus (Ad) encoding CD154 and/or treatment with ISS-ODN could enhance the capacity of A20 murine B lymphoma cells to function as APCs capable of inducing a syngeneic antilymphoma immune response. High-level expression of CD154 after infection with Ad-CD154 induced up-regulation of immune costimulatory molecules on A20 cells, as did incubation with ISS-ODN. Treatment of A20 cells with ISS-ODN also enhanced surface expression of alphav integrins, making them significantly more susceptible to Ad infection than nontreated A20 cells. In syngeneic mixed-lymphocyte reactions with BALB/c splenocytes, A20 cells activated with ISS-ODN and then transduced with Ad-CD154 were significantly more effective APCs than Ad-CD154 transduced cells, which, in turn, were significantly more effective than A20 cells treated with ISS-ODN alone. Also, injection of mice with ISS-activated, Ad-CD154-infected cells induced significantly better A20-specific immune responses against A20 cells, as assessed via enzyme-linked immunospot analysis in vitro and immune prophylaxis against subsequent challenge with A20 lymphoma cells in vivo. These data demonstrate that **CpG**-containing oligonucleotides can serve as an adjuvant for Ad-mediated gene therapy of B-cell malignancies.

L25 ANSWER 11 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5
AN 2003:281455 BIOSIS
DN PREV200300281455
TI A phase I study of the safety and immunogenicity of recombinant hepatitis B surface **antigen** co-administered with an **immunostimulatory** phosphorothioate **oligonucleotide** adjuvant.
AU Halperin, Scott A. (1); Van Nest, Gary; Smith, Bruce; Abtahi, Simin; Whitley, Heather; Eiden, Joseph J.
CS (1) Department of Pediatrics, Clinical Trials Research Center, IWK Health Centre, Dalhousie University, 5850 University Avenue, Halifax, NS, B3J 3G9, Canada: shalperin@iwkgrace.ns.ca Canada
SO Vaccine, (2 June 2003) Vol. 21, No. 19-20, pp. 2461-2467. print. ISSN: 0264-410X.
DT Article
LA English
AB Certain oligodeoxynucleotides with **CpG** motifs provide enhanced immune response to co-delivered antigens. We performed a phase I, observer-blinded, randomized study in healthy anti-hepatitis B surface **antigen** (anti-HBsAg) antibody negative adults to explore safety and immunogenicity of co-injection of recombinant HBsAg combined with an immunostimulatory DNA sequence (ISS) 1018 ISS. Four ISS dosage groups (N = 12 per group) were used: 300, 650, 1000 or 3000 mug. For each group, two controls received 20 mug HBsAg alone, two controls received ISS alone, and eight subjects received ISS +20 mug HBsAg. Subjects received two doses 8 weeks apart. Injection site reactions (tenderness and pain on limb movement) were more frequent at higher ISS + HBsAg doses but were mainly mild and of short duration. Higher anti-HBsAg antibody levels were associated with higher ISS doses. Four weeks after the first dose, a seroprotective titer (gtoreq 10 mIU/ml) was noted for 0, 25, 75, and 87.5% of subjects by increasing ISS dose group (P < 0.05) for those who received ISS+HBsAg; 1 month after the second dose this increased to 62.5, 100, 100, and 100%, respectively. Geometric mean anti-HBsAg antibody levels by increasing ISS + HBsAg dose were 1.22, 5.78, 24.75, and 206.5 mIU/ml after the first dose and 65.37, 877.6, 1545, and 3045 mIU/ml after the second dose. We conclude that 1018 ISS +HBsAg was well tolerated and immunogenic in this phase I study in healthy adults and may offer the potential for enhancement of hepatitis B virus (HBV) immunization and protection after one or two doses or in individuals who fail to respond to the standard vaccine regimen.

L25 ANSWER 12 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 6

AN 2003:308666 BIOSIS
DN PREV200300308666
TI Divergent synthetic nucleotide motif recognition pattern: Design and development of potent immunomodulatory oligodeoxyribonucleotide agents with distinct cytokine induction profiles.
AU Kandimalla, Ekambar R.; Bhagat, Lakshmi; Wang, Daqing; Yu, Dong; Zhu, Fu-Gang; Tang, Jimmy; Wang, Hui; Huang, Ping; Zhang, Ruiwen; Agrawal, Sudhir (1)
CS (1) Hybridon, Inc., 345 Vassar Street, Cambridge, MA, 02139, USA: sagrawal@hybridon.com USA
SO Nucleic Acids Research, (May 1 2003) Vol. 31, No. 9, pp. 2393-2400. print. ISSN: 0305-1048.
DT Article
LA English
AB Unmethylated **CpG** dinucleotides present within certain specific sequence contexts in bacterial and synthetic DNA stimulate innate immune responses and induce cytokine secretion. Recently, we showed that **CpG** DNAs containing two 5'-ends, immunomers, are more potent in both regards. In this study, we show that an immunomer containing a synthetic CpR motif (R=2'-deoxy-7-deazaguanosine) is a potent immunostimulatory agent. However, the profile of cytokine induction is different from that with immunomers containing a natural **CpG** motif. In general, a CpR immunomer induced higher interleukin (IL)-12 and lower IL-6 secretion. Compared with conventional **CpG** DNAs, both types of immunomers showed a rapid and enhanced activation of the transcription factor NF-kappaB in J774 cells. NF-kappaB activation by **CpG** DNA corresponded to degradation of IkappaBalpha in J774 cells. All three **immunostimulatory oligonucleotides** activated the p38 mitogen-activated protein kinase pathway as expected. Immunomers containing **CpG** and CpR motifs showed potent reversal of the **antigen**-induced Th2 immune response towards a Th1 type in **antigen**-sensitized mouse spleen cell cultures. Immunomers containing a CpR motif showed significant antitumor activity in nude mice bearing MCF-7 human breast cancer and U87MG glioblastoma xenografts. These studies suggest the ability for a divergent synthetic nucleotide motif recognition pattern of the receptor involved in the immunostimulatory pathway and the possibility of using synthetic nucleotides to elicit different cytokine response patterns.

L25 ANSWER 13 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 7
AN 2003:341255 BIOSIS
DN PREV200300341255
TI **Immunostimulatory CpG oligonucleotides** enhance the immune response of anti-idiotypic vaccine that mimics carcinoembryonic **antigen**.
AU Baral, Rathindra Nath; Saha, Asim; Chatterjee, Sunil K.; Foon, Kenneth A.; Krieg, Arthur M.; Weiner, George J.; Bhattacharya-Chatterjee, Malaya (1)
CS (1) Vontz Center for Molecular Studies, University of Cincinnati, 3125 Eden Avenue, Room 1316, Cincinnati, OH, 45267-0509, USA: malaya.chatterjee@uc.edu USA
SO Cancer Immunology Immunotherapy, (May 2003, 2003) Vol. 52, No. 5, pp. 317-327. print. ISSN: 0340-7004.
DT Article
LA English
AB We have developed and characterized a monoclonal anti-idiotypic (Id) antibody, designated 3H1, which mimics a specific epitope of carcinoembryonic **antigen** (CEA) and can be used as a surrogate for CEA. Anti-Id 3H1 induced anti-CEA immunity in different species of animals as well as humans and showed promise as a potential vaccine candidate in phase I/II clinical trials for colorectal cancer patients.

One area of interest to us has been the development of new immune adjuvants that may augment the potency of 3H1 as a tumor vaccine. Immunostimulatory oligonucleotides containing the unmethylated CpG motif (CpG ODN) are potent inducers of both innate and adaptive immunity and can serve as suitable vaccine adjuvants. In this study, using the CEA-transduced MC-38 murine colon carcinoma model in syngeneic C57BL/6 mice, we assessed whether a select CpG ODN (1826) can function as immune adjuvant in immunization of mice with anti-Id 3H1. Complete Freund's adjuvant (FA) was used as a gold standard in this system. A single immunization of 3H1 mixed with CpG ODN 1826 was sufficient to induce measurable anti-CEA immunity in naive mice. However, 3 immunizations every other week were necessary to obtain and sustain peak immune reactivity over a long period of time. With FA and 3H1, single immunization was ineffective and multiple immunizations (5 to 6) were needed to achieve and sustain peak immunity. Anti-CEA antibody reactivity was comparable in both groups, but cellular immune reactivity as measured by immune splenic lymphocyte T cell proliferation and cytotoxicity assay was slightly higher in the CpG ODN group. Mice immunized with 3H1 and either CpG ODN or FA were protected from challenge by lethal doses of MC-38-CEA cells. However, the degree of protection was slightly higher and the duration of survival was somewhat longer in the group of mice treated with 3H1 plus CpG ODN. Thus, CpG ODN 1826 was faster than FA in increasing anti-tumor immunity induced by anti-Id 3H1 immunization in this prophylactic model.

L25 ANSWER 14 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

AN 2003133341 EMBASE

TI Recent advances in the development of immunostimulatory oligonucleotides.

AU Uhlmann E.; Vollmer J.

CS E. Uhlmann, Coley Pharmaceutical GmbH, Elisabeth-Selbert-Strasse 9, D-40764 Langenfeld, Germany. euhlmann@coleypharma.com

SO Current Opinion in Drug Discovery and Development, (2003) 6/2 (204-217). Refs: 146

ISSN: 1367-6733 CODEN: CODDFP

CY United Kingdom

DT Journal; General Review

FS 004 Microbiology

016 Cancer

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LA English

SL English

AB Some immune cells recognize distinct molecular structures present in pathogens through specific pattern recognition receptors that are able to distinguish prokaryotic DNA from vertebrate DNA. The detection of invading microbial DNA is based on the recognition of unmethylated deoxycytidyl-deoxyguanosin dinucleotide (CpG) motifs. Synthetic oligonucleotides (ODNs) containing these CpG motifs are able to activate both innate and acquired immune responses through a signaling pathway involving Toll-like receptor 9 (TLR9). Depending on the sequence, length, as well as number and positions of CpG motifs in an ODN, distinct immunostimulatory profiles can be observed. These immunostimulatory profiles can be further modified and fine-tuned by appropriate chemical modifications, leading to preclinical and clinical development of CpG ODNs in cancer, allergy, asthma and infectious diseases.

L25 ANSWER 15 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 8

AN 2002-740766 [80] WPIDS

DNC C2002-209742

TI New isolated proteins capable of raising antibodies in humans, useful for treating interleukin-13 mediated diseases, e.g. asthma, allergies,

GA, GN, ML, MR, NE, SN, TD, TG

US 2002164341 A1 20021107 US 2001-23909 20011218
US 2003091599 A1 20030515 US 2002-300247 20021120
PRAI US 1997-40376P P 19970310
WO 1998-US4703 A2 19980310
US 1998-154614 A2 19980916
US 1999-325193 A3 19990603
US 2001-23909 A1 20011218
RE.CNT 173 THERE ARE 173 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 25 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 12
AN 2002207753 EMBASE
TI Vaccination with tumor peptide in **CpG** adjuvant protects via
IFN- γ -dependent CD4 cell immunity.
AU Stern B.V.; Boehm B.O.; Tary-Lehmann M.
CS Dr. M. Tary-Lehmann, Department of Pathology, Case Western Reserve
University, Biomedical Research Building, 10900 Euclid Avenue, Cleveland,
OH 44106, United States. mxt27@po.cwru.edu
SO Journal of Immunology, (15 Jun 2002) 168/12 (6099-6105).
Refs: 24
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English

L25 ANSWER 26 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:667624 CAPLUS
DN 138:71447
TI Synergistic adjuvant activity of immunostimulatory DNA and oil/water
emulsions for immunization with HIV p55 gag **antigen**
AU O'Hagan, D. T.; Singh, M.; Kazzaz, J.; Ugozzoli, M.; Briones, M.;
Donnelly, J.; Ott, G.
CS Chiron Corporation, Emeryville, CA, 94608, USA
SO Vaccine (2002), 20(27-28), 3389-3398
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 27 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:479170 CAPLUS
DN 137:92344
TI Binding immune-stimulating oligonucleotides to cationic peptides from
viral core **antigen** enhances their potency as adjuvants
AU Riedl, Petra; Buschle, Michael; Reimann, Jorg; Schirmbeck, Reinhold
CS Institute for Medical Microbiology and Immunology, University of Ulm, Ulm,
Germany
SO European Journal of Immunology (2002), 32(6), 1709-1716.
CODEN: EJIMAF; ISSN: 0014-2980
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 28 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:974858 CAPLUS

DN 138:105533
 TI Plasmacytoid dendritic cells: a new cutaneous dendritic cell subset with distinct role in inflammatory skin diseases
 AU Wollenberg, Andreas; Wagner, Moritz; Gunther, Sandra; Towarowski, Andreas; Tuma, Evelyn; Moderer, Martina; Rothenfusser, Simon; Wetzel, Stefanie; Endres, Stefan; Hartmann, Gunther
 CS Department of Dermatology and Allergy, University of Munich, Munich, Germany
 SO Journal of Investigative Dermatology (2002), 119(5), 1096-1102
 CODEN: JIDEAE; ISSN: 0022-202X
 PB Blackwell Publishing, Inc.
 DT Journal
 LA English
 RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 29 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:419032 BIOSIS
 DN PREV200200419032
 TI **Immunostimulatory CpG oligonucleotides**
 enhance the immune response of anti-idiotype vaccine that mimics carcinoembryonic **antigen**.
 AU Baral, Rathindra Nath (1); Chatterjee, Sunil K.; Saha, Asim; Das, Ruma; Foon, Kenneth A.; Krieg, Arthur M.; Weiner, George J.; Chatterjee, Malaya B.
 CS (1) University of Cincinnati, Cincinnati, OH USA
 SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 976. print.
 Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002
 ISSN: 0197-016X.
 DT Conference
 LA English

L25 ANSWER 30 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:343980 BIOSIS
 DN PREV200200343980
 TI Mucosal immune responses induced by **immunostimulatory oligonucleotides** are enhanced when formulated in lipid particles.
 AU Yuan, Zuan-Ning (1); Klimuk, Sandra K. (1); Semple, Sean C. (1)
 CS (1) Inex Pharmaceuticals Corp., 100-8900 Glenlyon Parkway, Burnaby, BC, V5J 5J8 Canada
 SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A680. /
<http://www.fasebj.org/>. print.
 Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
 ISSN: 0892-6638.
 DT Conference
 LA English

L25 ANSWER 31 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2002:343981 BIOSIS
 DN PREV200200343981
 TI CD8+ response induced by **CpG-peptide** may probably require CD4 help for maintenance.
 AU Gierynska, Malgorzata (1); Kumaraguru, Uday; Lee, Sujin; Rouse, Barry T.
 CS (1) Microbiology, University of Tennessee, 1414 Cumberland Avenue, Knoxville, TN, 37996 USA
 SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A680.
<http://www.fasebj.org/>. print.
 Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
 ISSN: 0892-6638.

TI Sterically stabilized cationic liposomes improve the uptake and
immunostimulatory activity of **CpG**
oligonucleotides.
 AU Gursel I; Gursel M; Ishii K J; Klinman D M
 CS Section of Retroviral Immunology, Center for Biologics Evaluation and
 Research, Food and Drug Administration, Bethesda, MD 20892, USA.
 SO JOURNAL OF IMMUNOLOGY, (2001 Sep 15) 167 (6) 3324-8.
 Journal code: 2985117R. ISSN: 0022-1767.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 200112
 ED Entered STN: 20010910
 Last Updated on STN: 20020122
 Entered Medline: 20011212

L25 ANSWER 42 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2001:630087 CAPLUS
 DN 135:317257
 TI Lactoferrin binds **CpG**-containing **oligonucleotides** and
 inhibits their **immunostimulatory** effects on human B cells
 AU Britigan, Bradley E.; Lewis, Troy S.; Waldschmidt, Mari; McCormick,
 Michael L.; Krieg, Arthur M.
 CS Research Service and Department of Internal Medicine, Veterans Affairs
 Medical Center, Iowa City, IA, 52246, USA
 SO Journal of Immunology (2001), 167(5), 2921-2928
 CODEN: JOIMA3; ISSN: 0022-1767
 PB American Association of Immunologists
 DT Journal
 LA English
 RE.CNT 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 43 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2001:258416 BIOSIS
 DN PREV200100258416
 TI The activation of APC in the CNS by microbial DNA controls whether the
 autoreactive memory T cells can cause EAE.
 AU Karulin, Alexey Y. (1); Darabi, Kamruz (1); Hoffstetter, Harald H. (1);
 Chavez, Guan C. (1); LaManna, Joseph C. (1); Fabry, Zsuzsanna (1);
 Lehmann, Paul V. (1)
 CS (1) Case Western Reserve University, 2109 Adelbert Rd., Cleveland, OH,
 44106 USA
 SO FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1057. print.
 Meeting Info.: Annual Meeting of the Federation of American Societies for
 Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA
 March 31-April 04, 2001
 ISSN: 0892-6638.
 DT Conference
 LA English
 SL English

L25 ANSWER 44 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 2001:267698 BIOSIS
 DN PREV200100267698
 TI **CpG** ODN can promote Th1 type immune responses and can re-direct
 pre-established Th2 responses in adult and young mice.
 AU Weeratna, Risini D. (1); McCluskie, Michael J. (1); Brazolot-Millan,
 Cynthia L.; Davis, Heather L. (1)
 CS (1) Coley Pharmaceutical Canada, 725 Parkdale Avenue, Ottawa, ON, K1Y 4E9
 Canada
 SO FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A652. print.

Meeting Info.: Annual Meeting of the Federation of American Societies for
Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA
March 31-April 04, 2001
ISSN: 0892-6638.

DT Conference
LA English
SL English

L25 ANSWER 45 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:267696 BIOSIS
DN PREV200100267696

TI Optimization of anti-HIV immune responses using **immunostimulatory**
sequence **oligonucleotide** vaccines.

AU Datta, Sandip K. (1); Horner, Anthony A. (1); Takabayashi, Kenji (1);
Hayashi, Tomoko (1); Richman, Douglas D. (1); Raz, Eyal (1)
CS (1) University of California, San Diego, 9500 Gilman Drive, La Jolla, CA,
92093-0663 USA

SO FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A652. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for
Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA
March 31-April 04, 2001
ISSN: 0892-6638.

DT Conference
LA English
SL English

L25 ANSWER 46 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:220169 BIOSIS
DN PREV200200220169

TI ISS-oligonucleotide treated A20 cells have enhanced susceptibility to
adenovirus (Ad) infection and become highly-efficient **antigen**
-presenting cells when infected with Ad-CD154 encoding the CD40-ligand.

AU Rieger, Roman (1); Kipps, Thomas J. (1)
CS (1) School of Medicine, Division of Hematology/Oncology, University of
California, San Diego, La Jolla, CA USA

SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 609a.
<http://www.bloodjournal.org/>. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.

DT Conference
LA English

L25 ANSWER 47 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2001277545 EMBASE

TI Effect of **immunostimulatory CpG-**
oligonucleotides in chronic lymphocytic leukemia B cells.

AU Decker T.; Peschel C.

CS Dr. C. Peschel, IIIrd Department of Medicine, Technical University of
Munich, Ismaninger Str. 15, 81675 Munich, Germany.
christian.peschel@lrz.tum.de

SO Leukemia and Lymphoma, (2001) 42/3 (301-307).
Refs: 77

ISSN: 1042-8194 CODEN: LELYEA

CY United Kingdom

DT Journal; General Review

FS 016 Cancer
025 Hematology
030 Pharmacology
037 Drug Literature Index

LA English
SL English

PB American Association of Immunologists
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L25 ANSWER 62 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 26
AN 2001:62072 BIOSIS
DN PREV200100062072
TI Bacterial **CpG**-DNA activates dendritic cells in vivo: T helper
cell-independent cytotoxic T cell responses to soluble proteins.
AU Sparwasser, Tim; Vabulas, Ramunas M.; Villmow, Brigitte; Lipford, Grayson
B.; Wagner, Hermann (1)
CS (1) Institute of Medical Microbiology, Immunology and Hygiene, Technical
University of Munich, Trogerstr. 9, D-81675, Munich: h.wagner@lrz.tu-
muenchen.de Germany
SO European Journal of Immunology, (December, 2000) Vol. 30, No. 12, pp.
3591-3597. print.
ISSN: 0014-2980.
DT Article
LA English
SL English
- L25 ANSWER 63 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 27
AN 2000:198103 BIOSIS
DN PREV2000000198103
TI **CpG** DNA overcomes hyporesponsiveness to hepatitis B vaccine in
orangutans.
AU Davis, Heather L. (1); Suparto, Irma; Weeratna, Risini; Jumintarto;
Iskandriati, Diah; Chamzah, Siti; Ma'ruf, Amir; Nente, Citrakasih;
Pawitri, Dyah; Krieg, Arthur M.; Heriyanto; Smits, Willie; Sajuthi, Dondin
CS (1) Loeb Health Research Institute at the Ottawa Hospital, 725 Parkdale
Avenue, Ottawa, ON, K1Y 4E9 Canada
SO Vaccine, (March 17, 2000) Vol. 18, No. 18, pp. 1920-1924.
ISSN: 0264-410X.
DT Article
LA English
SL English
- L25 ANSWER 64 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 28
AN 2000042632 EMBASE
TI **Immunostimulatory CpG-oligonucleotides** cause
proliferation, cytokine production, and an immunogenic phenotype in
chronic lymphocytic leukemia B cells.
AU Decker T.; Schneller F.; Sparwasser T.; Tretter T.; Lipford G.B.; Wagner
H.; Peschel C.
CS C. Peschel, IIIrd Department of Medicine, Technical University of Munich,
Ismaninger Str. 15, 81675 Munich, Germany. christian.peschel@lrz.tu-
muenchen.de
SO Blood, (1 Feb 2000) 95/3. (999-1006).
Refs: 42
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 016 Cancer
025 Hematology
LA English
SL English
- L25 ANSWER 65 OF 82 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

AN 2001-01035 BIOTECHDS
 TI **CpG** DNA is an effective oral adjuvant to protein antigens in mice;
 oligonucleotide containing immunostimulatory
 CpG motif useful as vaccine adjuvant
 AU McCluskie M J; Weeratna R D; Krieg A M; *Davis H L
 CS Loeb-Health-Res.Inst.Ottawa; Univ.Iowa; Univ.Ottawa; Coley-Pharmaceutical
 LO Loeb Health Research Institute at the Ottawa Hospital, 725 Parkdale
 Avenue, Ottawa, Ontario, Canada K1Y 4E9
 Email: hdavis@lri.ca
 SO Vaccine; (2000) 19, 7-8, 950-57
 CODEN: VACCDE ISSN: 0264-410X
 DT Journal
 LA English

L25 ANSWER 66 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 AN 2000221186 EMBASE
 TI **CpG** motifs induce Langerhans cell migration in vivo.
 AU Ban E.; Dupre L.; Hermann E.; Rohn W.; Vendeville C.; Quatannens B.;
 Ricciardi-Castagnoli P.; Capron A.; Riveau G.
 CS E. Ban, INSERM U167, Institut Pasteur de Lille, 59019 Lille Cedex, France
 SO International Immunology, (2000) 12/6 (737-745).
 Refs: 44
 ISSN: 0953-8178 CODEN: INIMEN
 CY United Kingdom
 DT Journal; Article
 FS 013 Dermatology and Venereology
 026 Immunology, Serology and Transplantation
 LA English
 SL English

L25 ANSWER 67 OF 82 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
 DUPLICATE 29
 AN 2000167542 EMBASE
 TI **Immunostimulatory CpG-oligonucleotides**
 induce functional high affinity IL-2 receptors on B-CLL cells:
 Costimulation with IL-2 results in a highly immunogenic phenotype.
 AU Decker T.; Schneller F.; Kronschnabl M.; Dechow T.; Lipford G.B.; Wagner
 H.; Peschel C.
 CS Dr. C. Peschel, IIIrd Department of Medicine, Technical University of
 Munich, Ismaninger Str. 15, 81675 Munich, Germany.
 christian.peschel@lrz.tu-muenchen.de
 SO Experimental Hematology, (2000) 28/5 (558-568).
 Refs: 40
 ISSN: 0301-472X CODEN: EXHEBH
 PUI S 0301-472X(00)00144-2
 CY United States
 DT Journal; Article
 FS 005 General Pathology and Pathological Anatomy
 016 Cancer
 025 Hematology
 LA English
 SL English

L25 ANSWER 68 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 30
 AN 2000:155296 BIOSIS
 DN PREV200000155296
 TI The effects of DNA containing **CpG** motif on dendritic cells.
 AU Behboudi, S. (1); Chao, D.; Klenerman, P.; Austyn, J.
 CS (1) Nuffield Department of Surgery, University of Oxford, John Radcliffe
 Hospital, Oxford, OX3 9DU UK
 SO Immunology., (March, 2000) Vol. 99, No. 3, pp. 361-366.

related diseases using **CpG** oligonucleotides

IN Gramzinski, Robert A.; Krieg, Arthur M.; Davis, Heather L.; Hoffman, Stephen L.
PA University of Iowa Research Foundation, USA; Ottawa Civic Loeb Research Institute; United States Dept. of the Navy
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9956755	A1	19991111	WO 1999-US9863	19990506
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2328602	AA	19991111	CA 1999-2328602	19990506
	AU 9938841	A1	19991123	AU 1999-38841	19990506
	EP 1077708	A1	20010228	EP 1999-921705	19990506
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
PRAI	US 1998-84512P	P	19980506		
	WO 1999-US9863	W	19990506		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 76 OF 82 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 33
AN 1999:428745 BIOSIS
DN PREV199900428745
TI The effect of **CpG** sequences on the B cell response to a viral glycoprotein encoded by a plasmid vector.
AU Pasquini, S.; Deng, H.; Reddy, S. T.; Giles-Davis, W.; Ertl, H. C. J. (1)
CS (1) Wistar Institute, 3601 Spruce Street, Philadelphia, PA, 19104 USA
SO Gene Therapy, (Aug., 1999) Vol. 6, No. 8, pp. 1448-1455.
ISSN: 0969-7128.
DT Article
LA English
SL English

L25 ANSWER 77 OF 82 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AN 1999-04201 BIOTECHDS
TI Immunoadjuvant action of plasmid DNA in liposomes;
plasmid pRc/CMV HBS encoding hepatitis B small protein surface
antigen lipofection into mouse, useful for optimization of
nucleic acid vaccine immune response
AU Gursel M; Tunca S; Ozkan M; Ozcengiz G; Alaeddinoglu G
CS Univ.Middle-East-Tech.
LO FDA, Division of Viral Products, Room 3D22, Building 29A, Bethesda, MD 20892, USA.
Email: ihsangursel@hotmail.com
SO Vaccine; (1999) 17, 11-12, 1376-83
CODEN: VACCDE ISSN: 0264-410X
DT Journal
LA English

L25 ANSWER 78 OF 82 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

Sparwasser et al.

Lipford, Grayson B.; Ellwart, Joachim W.; Wagner, Hermann (1)
 CS (1) Inst. Med. Microbiol., Immunol. Hygiene, Trogerstr. 9, D-81675 Munich
 Germany
 SO European Journal of Immunology, (June, 1998) Vol. 28, No. 6, pp.
 2045-2054.
 ISSN: 0014-2980.
 DT Article
 LA English

L25 ANSWER 81 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1997:361702 CAPLUS
 DN 126:326443
 TI Genetic vector expression system for vaccination of fish by immersion,
 injection, or spray and fish protection from viral and bacterial diseases
 IN Davis, Heather L.
 PA Ottawa Civic Hospital, Can.
 SO Eur. Pat. Appl., 15 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 773295	A2	19970514	EP 1996-117859	19961107
	EP 773295	A3	19990616		
	R: DK, FI, FR, GB, SE				
	US 5780448	A	19980714	US 1996-740805	19961104
	CA 2189831	AA	19970508	CA 1996-2189831	19961107
	NO 9604713	A	19970509	NO 1996-4713	19961107
	JP 09295291	A2	19971104	JP 1996-295565	19961107
	EP 839913	A2	19980506	EP 1997-119273	19971104
	EP 839913	A3	19990616		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6180614	B1	20010130	US 1998-115423	19980714
PRAI	US 1995-6290P	P	19951107		
	US 1996-740805	A	19961104		
	EP 1996-117859	A	19961107		

L25 ANSWER 82 OF 82 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1998:25971 CAPLUS
 DN 128:87598
 TI Immunostimulatory DNA. Sequence-dependent production of potentially
 harmful or useful cytokines
 AU Lipford, Grayson B.; Sparwasser, Tim; Bauer, Marc; Zimmermann, Stefan;
 Koch, Eva Sophie; Heeg, Klaus; Wagner, Hermann
 CS Institute Medical Microbiology, Immunology Hygiene, Technical University
 Munich, Munich, D-81675, Germany
 SO European Journal of Immunology (1997), 27(12), 3420-3426
 CODEN: EJIMAF; ISSN: 0014-2980
 PB Wiley-VCH Verlag GmbH
 DT Journal
 LA English

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
300.84	451.76

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-5.86	-20.18

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